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Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme

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Summary

After the success of a controlled trial of insecticide-treated bednets in lowering child mortality, The Gambia initiated a National Insecticide Impregnated Bednet Programme (NIBP) in 1992 with the objective of introducing this form of malaria control into all large villages in The Gambia.

Five areas (population 115 895) were chosen as sentinel sites for evaluation of the NIBP. During the first year of intervention a 25% reduction was achieved in all-cause mortality in children 1–9 years old living in treated villages (rate ratio 0·75 [95% CI 0·57–0·98], p=0·04). If one area where the programme was ineffective was excluded, the reduction was 38% (0·62 [0·46–0·83), p=0·001). A decrease in rates of parasitaemia and high-density parasitaemia, an increase in mean packed-cell volume (rate ratio 0·75 [95% CI 0·59–0·98], p=0·04) and an improvement in the nutritional status of children living in treated villages were also detected.

In a country such as The Gambia, where nets were widely used and which has a good primary health care system, it is possible to achieve insecticide-treatment of bednets at a national level with a significant reduction in child mortality; but at a cost which the country cannot afford.

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Introduction

In The Gambia malaria remains one of the most common causes of death among children less than 5 years old. In 1988–89 the malaria mortality rate among Gambian children in this age group was estimated to be 6·1 per 1000 and it is likely that at least 1000 Gambian children die from malaria each year.[1]

After promising results from small-scale trials undertaken with untreated and treated bednets,[2,3] a large controlled trial, combined with a short period of chemoprophylaxis given during the period of maximum malaria transmission, was undertaken in a population of 20 000 in central Gambia.[4] Sleeping under insecticide-impregnated bednets was associated with a reduction in overall mortality of about 60% in children 1–4 years old.[5,6] Episodes of fever associated with malaria parasitaemia were reduced by 45%; splenomegaly, parasitaemia, high-density parasitaemia rates at the end of the malaria transmission season were reduced by 35%, 39%, and 48%. On the basis of this result, the Government of The Gambia, with support from WHO, initiated a National Insecticide Impregnated Bednet Programme (NIBP) with the objective of introducing this form of malaria control into all large villages in The Gambia over a 2–3 year period. The UK Medical Research Council laboratories were asked to evaluate the impact on childhood mortality and malaria morbidity in order to determine whether the results achieved in the controlled trial could be reproduced in a nationwide programme.

Subjects and methods

Study area

Epidemiological characteristics of malaria in The Gambia have been described.[7] Malaria is seasonal with moderate transmission (1–10 infective bites per year) occurring during a few months of the rainy season (July–December). The dominant parasite is *Plasmodium falciparum* and the dominant vector *Anopheles gambiae*.[8]

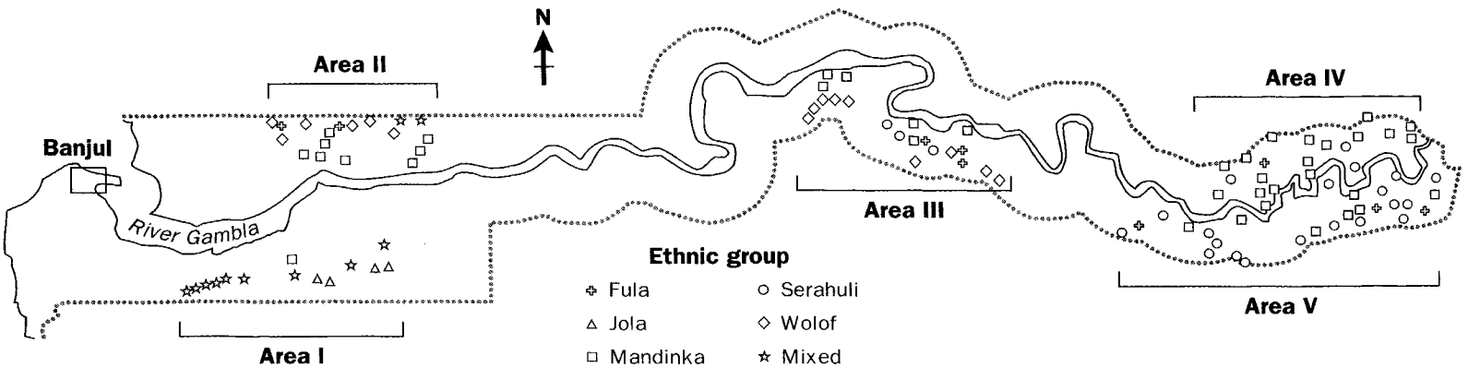

Figure 1: **Map of The Gambia showing 5 study areas, villages under surveillance and main ethnic group**

National impregnated bednet programme

In 1981, The Gambian Government initiated a national Primary Health Care (PHC) programme; all villages with a population of 400 or more were invited to join the scheme. Each participating village selected a village health worker and a traditional birth-attendant who received 6 and 8 weeks' training, respectively. In June–July, 1992, the NIBP was implemented in about half (221) of the PHC villages. Dipping of bednets was organised by Regional Health Teams and done by a village health worker assisted by a traditional birth-attendant and the head of the women's group, supervised by community health nurses. Before the intervention, people were asked to wash their nets. 40 mL insecticide (20% permethrin) needed to treat each net was poured into a large plastic bowl and 2 litres of water added to give a permethrin concentration on nets of about 200 mg/m^2.

Evaluation

Since the objective was to measure the effectiveness of the programme, villages with and without the intervention were compared. At the beginning of 1991, five areas were chosen as sentinel sites (figure 1) to reflect the varied cultural and ecological settings within The Gambia.[7] Within these areas, 104 PHC villages were identified and the project was discussed with villagers. The villages were then paired by size (1983 national census) within each area. The intervention was implemented in one randomly chosen village in each pair (treated village) in June–July, 1992, and in the other the following year. A census of the villages under surveillance was done in March–May, 1992. During the census, the numbers of children born and children surviving were collected from women of reproductive age, and the number of beds with hanging nets recorded.

Prospective demographic surveillance was started in 81 villages on Aug 1, 1991, one year before implementation of the treatment programme, and continued until the end of the evaluation. Because mortality rates were lower in 1991–92 than expected, 23 new villages were added in March, 1992, these 104 villages representing approximately 25% of all PHC villages (table 1). All deaths in the villages under surveillance were recorded by village reporters and this information was collected and checked weekly by Medical Research Council field assistants. Mortality data were checked by yearly re-enumeration of the villages under surveillance. From August, 1992, the parents or guardians of all dead children were visited by a senior field assistant who administered a questionnaire about the circumstances of the child's death.[9,10] Questionnaires were analysed independently by three doctors unaware of the village and bednet status of the dead child. A probable cause of death was accepted if this was agreed by at least two of the three.

Morbidity surveys were done at the end of the 1991 rainy season (pre-intervention) and at the end of the 1992 rainy season (post-intervention). Each year, 1500 children, half from treated and half from untreated villages, were sampled, 300 in each area. 5 treated and 5 untreated villages were chosen with probability proportional to size within each area. Compounds in chosen villages were then selected randomly and all children aged 1–4 years living in the compound were sampled until 30 children were recruited in each village (60 if villages were sampled twice). Clinical examination was done, anthropometric measurements made (only in 1992), body temperature recorded, and a blood sample collected by finger-prick for determination of packed-cell volume (PCV) and preparation of thick and thin blood films. Thick films were stained and examined as previously described.[10] All children with a positive thick blood film and/or PCV of 25% or less were treated with chloroquine and/or iron and folic acid. Information on chloroquine consumption was collected from health cards, and questions were asked on bednet use by study children.

Analysis

All-cause and malaria-specific mortality were analysed by intention to treat, and a multivariate Poisson regression model[12] was fitted. Data from a pair of communities were represented as two correlated observations on that pair, and the model included a fixed treatment effect. The model allowed for the confounding effects (at community level) of predominant ethnic group, percentage of bednet usage, distance from the river, and pre-intervention mortality. Pre-intervention mortality and infant

	Area				
	1	2	3	4	5
No of villages	14	18	21	23	28
Population					
Total	13 163	16 808	20 555	21 393	43 975
Aged 1–4 yrs	1882	2759	3445	3446	7379
Aged 5–9 yrs	2132	3000	3691	3857	8511
Beds with nets (%)	58·6	61·3	78·6	48·2	46·4
Ethnic group (%)					
Mandinka	29·1	62·2	33·3	66·8	15·2
Wollof	2·7	24 6	30·0	0·2	0·1
Jola	45·5	0·6	0·7	0·1	0·1
Fula	12·8	10·0	16·6	4·9	10·8
Serere	2·0	1·4	0·2	0·0	0·0
Serahuli	2·4	0·4	18 2	27·9	73·2
Others	5·5	0·8	0 9	0·0	0·6

Table 1: **Demography**

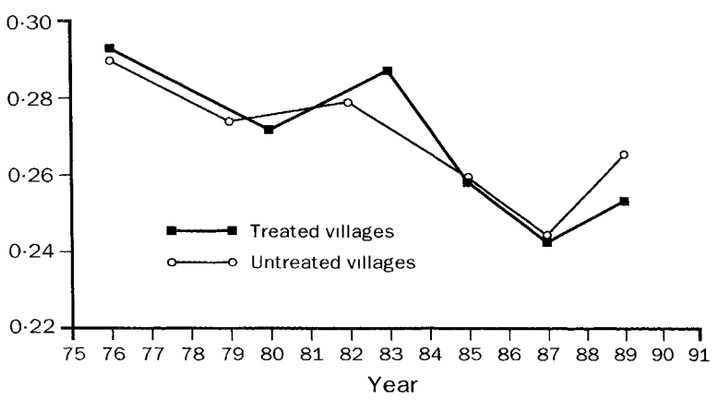

Figure 2: **Probability of death before age 5 years**

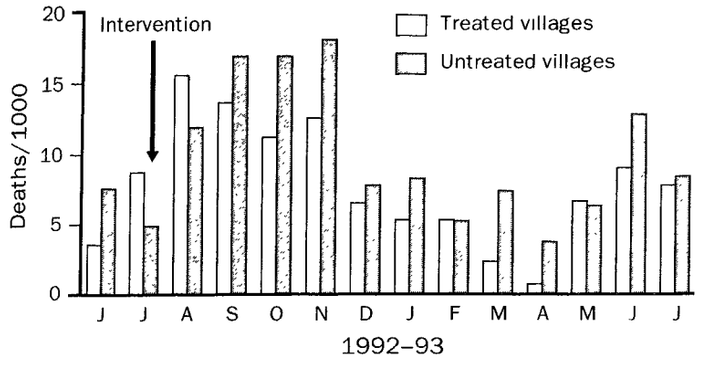

Figure 3: **Mortality rates by month in treated and untreated villages**

mortality data were stratified by area and a Mantel-Haenszel rate ratio (RR) and test statistic were calculated.

Morbidity prevalence was analysed by a logistic-binomial regression model[13] to account for clustering of the sample of children by community. The model allowed for the confounding effects of area and of the sex, age, and ethnic group. Mean PCV were compared by an analysis of variance of village means, allowing for area. Anthropometic measures were computed as *z*-scores and mean scores[14] analysed by ANOVA.

Results

Population under surveillance and bednet use

During the first census of the five study areas undertaken in March–May, 1992, 115 895 people were counted, of whom 18 911 were children aged 1–4 and 21 191 children aged 5–9 years. Use of bednets was not uniform, area 3 having the highest and area 5 the lowest (table 1) percentage of beds with nets. Ethnic group composition also varied between areas.

Mortality in treated and untreated villages

Under-5 mortality, as determined by questionnaire, in the intervention and control groups of villages was very similar in the 1976–89 period before the intervention (figure 2). However, the pattern of change for both intervention and control villages varied by area. A pronounced and steady decrease in mortality was observed in areas 1–3 but little change in areas 4 and 5 (data not shown).

Mortality rates in children under 9 were determined during the intervention and pre-intervention years by prospective surveillance. During the pre-intervention year, mortality rates were somewhat higher in the villages scheduled to be treated in 1992 (rate ratio 1·22, 95% CI 0·97–1·54, p=0·08), particularly in areas 4 and 5 (data not shown). After the intervention, mortality in treated villages fell approximately 1 month after nets were dipped; the difference between groups was greater in October and November when most malaria deaths occur (figure 3).

	Age			
	1–2 yrs	3–4 yrs	5–9 yrs	All ages
RR	0·95	0·55	0·53	0·75
95% CI	0·71–1·28	0·30–1·01	0·28–0·99	0·57–0·98
z	0·31	1·94	1·98	2·09
p	0·75	0·05	0·05	0·04

Table 3: **Rate ratio (RR) from multivariate Poisson model**

The treatment of nets was associated with a reduction in all-cause mortality in all age groups in all areas, with the exception of children aged 1–2 years in area 5 (table 2). Overall, a 25% reduction in mortality in children aged 1–9 years (p=0·04) was seen in treated villages (table 3). If area 5 is excluded, a 38% (RR 0·62, 0·46–0·83, p=0·001) reduction in mortality was found. After the intervention, infant mortality rate ([deaths under 1 year of age/number of livebirths]×1000) was significantly lower in treated (179/2848, 63 per 1000) than in untreated villages (241/3062, 83 per 1000) (0·81; [0·70–0·95], p=0·04). Reduction in mortality was greater if children younger than 1 month, an age group in which death from malaria is very unlikely, were excluded (post-neonatal mortality rate)—treated villages 88/2848, 31 per 1000; untreated villages 131/3062, 43 per 1000 (0·74, [0·60–0·92] p=0·03). In the year before intervention, the groups of villages had similar post-neonatal mortality rates (1·17 [1·51–0·91] p=0·32).

Bednet use in a village had a significant effect on mortality independently of insecticide impregnation: a reduction of 8% (1%–12%, p=0·01) was found for every 10% increase in net usage. Among village pairs and after adjustment for age, the effect of the intervention was inversely associated with the mortality rate in that pair before the intervention (partial correlation of log rate ratio with log geometric mean mortality rate, −0·14, p=0·10). In the pre-intervention year the age-adjusted correlation was 0·04 (p=0·68).

Questionnaires from parents were obtained for 79% (316/397) of dead children. 4 deaths diagnosed as malaria/acute respiratory infection are classified as malaria deaths. Overall, a 14% reduction in malaria mortality in children aged 1–9 years old (0·86 [0·60–1·23], p=0·40) was detected in treated villages (table 4). If area 5 is excluded, the rate ratio for all age groups was 0·67 (0·44–1·02, p=0·06), a 33% reduction. Non-malaria mortality rates follow the same pattern. In untreated villages, 54% (47/86) of deaths in children 3–9 years old were attributed to malaria, and in children 1–2 years old, 36% (38/104) deaths were attributed to malaria (p=0·02).

Morbidity

67% (603/794) of children resident in treated villages regularly slept under insecticide-impregnated bednets.

Area	Age								
	1–2 years old			3–4 years old			5–9 years old		
	Treated	Untreated	RR	Treated	Untreated	RR	Treated	Untreated	RR
1	5·8 (3/514)	14·1 (7/495)	0·41	1·8 (1/542)	5·8 (3/513)	0·31	0·8 (1/1204)	1·6 (2/1190)	0·50
2	11·7 (9/768)	22·7 (16/704)	0·51	5·7 (4/704)	13·4 (9/670)	0·42	3·8 (6/1578)	5·0 (8/1584)	0·76
3	14·4 (14/970)	24·8 (22/884)	0·58	4·2 (4/938)	13·3 (11/833)	0·31	2·8 (6/2079)	5·9 (11/1862)	0·47
4	31·3 (31/988)	29·5 (25/847)	1·05	4·2 (4/951)	8 4 (7/829)	0·50	1·8 (4/2129)	2·5 (5/1971)	0·72
5	33·3 (51/1531)	23·3 (54/2316)	1·42	9·7 (15/1548)	12·5 (29/2316)	0·81	2·6 (9/3463)	4·5 (26/5678)	0·57
All	22·6 (108/4771)	23·6 (124/5246)	0·95	5·9 (28/4683)	11·4 (59/5161)	0·52	2·5 (26/10 453)	4·2 (52/12 285)	0·59

Table 2: **Mortality rates (deaths/child years) and rate ratios (RR) (treated:untreated) by age group and area in post-intervention year (1992–93)**

Area	Treated villages		Untreated villages		Rate ratio	
	Malaria	Non-malaria	Malaria	Non-malaria	Malaria	Non-malaria
1	2·2 (5/2260)	0 (0/2260)	0·9 (2/2199)	3·2 (7/2199)	2·44	0·00
2	3·3 (11/3050)	1·6 (5/3050)	5·4 (17/2958)	2·0 (6/2958)	0·61	0·80
3	2·0 (8/3988)	2·2 (9/3988)	4·4 (16/3580)	5·6 (20/3580)	0·45	0·39
4	2·9 (12/4069)	3·7 (15/4069)	3·5 (13/3647)	4·1 (15/4069)	0·83	0·90
5	4·3 (28/6544)	4·7 (31/6544)	3 3 (37/10 407)	4·7 (49/10 407)	1·30	1·00
All	3·2 (64/19 911)	3·0 (60/19 912)	3·7 (85/22 791)	4·2 (97/22 792)	0·86	0·71

Table 4: **Malarial and non-malarial (excluding trauma) specific mortality rates in children 1–9 years old during post-intervention year (1992–93)**

Area	Number/total (%) of children with:						Mean (SD) PCV	
	Parasitaemia		High-density parasitaemia		Splenomegaly		Treated	Untreated
	Treated	Untreated	Treated	Untreated	Treated	Untreated		
1	44/156 (28·2)	54/147 (36·7)	9/156 (5·7)	22/147 (15·0)	7/156 (4·5)	18/147 (12·2)	34·7 (3·9)	33·8 (3·4)
2	29/127 (22·8)	43/130 (33·0)	11/127 (8·7)	18/130 (13·8)	19/127 (15·0)	16/130 (12·3)	34·2 (3·9)	34·2 (4·7)
3	28/176 (15·9)	37/143 (25·8)	8/176 (4·5)	17/143 (11·9)	17/176 (9·6)	21/143 (14·6)	33·3 (3·8)	31·9 (4·3)
4	82/190 (43·1)	65/122 (53·3)	22/190 (11·5)	24/122 (19·7)	33/190 (17·4)	22/122 (23·0)	32·1 (5·2)	31·1 (5·6)
5	105/148 (71·0)	81/181 (44·7)	44/148 (29·7)	16/181 (8·8)	55/148 (37·2)	55/181 (30·3)	30·6 (4·5)	31·8 (4·9)
All	288/797 (36·1)	280/723 (38·7)	94/797 (11·8)	97/723 (13·4)	131/797 (16·4)	138/723 (19·1)	32·9 (4·6)	32·6 (4·7)

Table 5: **Rates of parasitaemia, high-density parasitaemia: (5000 parasites/μl or more), splenomegaly, and mean PCV after intervention**

This percentage varied from area to area, area 2 having the highest coverage (94%) and area 5 the lowest (56%).

Table 5 shows the percentage of children in treated and untreated villages with parasitaemia, high-density parasitaemia, and splenomegaly after the intervention, and their mean PCV. In the pre-intervention survey there were no significant differences between the groups of villages. Overall there were non-significant reductions in the percentage of parasitaemia, high-density parasitaemia, and splenomegaly in treated villages (odds ratio 0·75, 0·76, and 0·82) and a non-significant increase in PCV (0·49%). However, if area 5 is excluded from the analysis there was a statistically significant reduction of about 50% in parasitaemia and high-density parasitaemia rates and an increase of 0·9% in mean PCV.

After the intervention, the mean z-scores of weight-for-age and weight-for-height were higher in children from treated (−1·36; −0·98) than in those from untreated villages (−1·46; −1·13), differences that are statistically significant after allowance for area, age, bednet use, and sex (p=0·008; p=0·001). The mean z-score of height-for-age was similar in the 2 groups of children (−0·92 and −0·89, p=0·6).

Information on chloroquine consumption was collected for 1081 children. 26% (152/578) of children in treated and 24% (119/503) in untreated villages had received one or more courses of chloroquine between Aug 1, 1992, and the day of the survey.

Discussion

Although studies have shown that insecticide-treated bednets are effective at preventing malaria, it cannot be assumed that control measures of this kind will be effective when introduced as a national public health measure.[15] The difficulties of distributing insecticide at the right time of the year, of ensuring that insecticide is used at the correct dilution, and of treating all the nets in a village are substantial. The NIBP employed a manager (MKC), responsible for coordinating the programme, purchasing the insecticide, organising the health education campaign, and liasing with the different RHTs. However, at the local level, the NIBP was organised and implemented mainly by rural health teams. Despite the many logistical problems encountered, mortality in children was reduced significantly in villages where bednets were used and treated with insecticide, indicating that in these age groups, malaria is the most important cause of death, a view supported by review of post-mortem questionnaires. In children 1–2 years old there was a reduction in mortality in four areas but not overall, because of the results from area 5 where mortality rates were higher in treated than in untreated villages. A decrease in parasitaemia and high-density parasitaemia rates was also detected in all areas except in area 5, where the rates were higher in treated than in untreated villages.

To evaluate the programme rather than the effectiveness of nets per se, analysis was on intention to treat rather than on individual protection. The overall reduction in mortality and morbidity was less than that observed in the controlled trial[5,6] but when analysed by individual use of nets the effect was greater (data not shown). There are several explanations. The intervention did not have the expected impact in area 5, where mortality in one age group was higher in treated than in untreated villages. Furthermore, when the NIBP was planned, it was assumed that the level of bednet use throughout the country would be similar to that found in the area where the controlled trial was done and where 96% of children 1–4 years old regularly slept under a net.[6] This was not the case, and a nationwide survey[16] on bednet usage found that only about 70% of children 1–4 years old regularly slept under a bednet. Considering that the NIBP treated about 80% of the existing nets, it is likely that in treated villages only about 60% of children 1–4 years old slept under a treated net, a figure well below that found in the controlled trial.[6] Thus detection of an overall reduction in mortality in children 1–9 years old of 25% (38%, excluding area 5) is in keeping with the findings of the previous study in which a 60% reduction in mortality was found. In contrast to the situation in the controlled trial, some insecticide may have been passed from treated to control villages, thus reducing the difference between the 2 groups.

The intervention was not successful in area 5, particularly in children 1–2 years old. No evidence of insecticide resistance was found but, in the pre-intervention year, area 5 had the highest entomological inoculation rate, mainly because of the very high

sporozoite rate in *A gambiae* in this area.[7] A subsequent observational study (unpublished) has shown low usage of nets by children in this area. These two factors may partly explain the lack of impact on mortality and morbidity in area 5.

It was not possible to show a selective effect on mortality attributed to malaria because deaths due to other causes fell in villages with insecticide-treated nets, as noted previously.[5] This finding may be due in part to the difficulty in differentiating deaths from malaria from those of other infections, such as pneumonia, by questionnaire.[9] However, it probably also reflects the fact that reducing the prevalence of malaria has an indirect beneficial effect on deaths from other infections such as pneumonia[17] and malnutrition, a view supported by the fact that children in villages with treated nets were better nourished than those in untreated villages.

We have shown that, in a country where nets are widely used and which has a good primary health care system, it is possible to achieve insecticide treatment of bednets at a national level with a satisfactory reduction in child mortality. However, there is the problem of cost. The 1992 NIBP campaign cost about US$92 000, 60% of which was attributed to the cost of insecticide. Annual cost of insecticide needed to treat all bednets in The Gambia would be about US$150 000, a sum beyond the means of the Gambian Ministry of Health. In 1993 a cost-recovery programme was introduced and villages given free insecticide during the first year of the study were asked to pay 5·00 Dalasi (US$0·5) per bednet treated. Unfortunately this led to a dramatic drop in coverage and a return of child mortality rates in these villages to their pre-intervention values.

In 1992, the estimated cost of death averted was about US$600, a sum that compares favourably with other successful health interventions such as measles vaccination and oral rehydration solutions (in preparation). Therefore, even on a national scale, insecticide treatment of bednets is a cost-effective method of malaria control. Finding new ways of financing such programmes is now a matter of priority.

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