Effectiveness of a lambda-cyhalothrin bednet impregnation against forest/border malaria in northwest Thailand.

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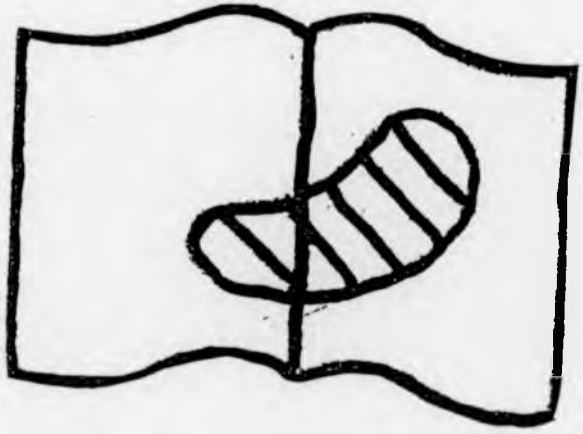

ABSTRACT

A cohort study was carried out in Mae Sariang district close to Thai-Myanmar border. This was aimed at measuring the pattern and size of movements as well as their relevance to malaria illness. Overall 494 people in 95 households were randomly selected from 5 small villages. They were fortnightly visited and interviewed by interpreters on the details of activities causing them to spend nights outside the village. A malaria illness was detected by the case detection systems already available. The results showed that short term movements during the transmission season were common. About 74% of villagers moved at least once. An average of 11% of their nights were spent outside the villages. Adult males predominated. The commonest and second most common reasons for movements were agricultural (41%) and forest (17%) activities respectively. Movements carried a 7.8 times higher risk than staying in the village ($p < 0.01$). Forest work (including illegal) had about 6 times higher risk than the other activities ($p < 0.05$).

A randomise placebo control trial of a lambda-cyhalothrin bednet impregnation, on a community basis, was also carried out in the same area. This was aimed at measuring the effectiveness of the insecticide treated bednet programme and involved 12 pairs of small villages, called bans in Thai. The outcome measure was a malaria incidence, detected by the existing case detection system, and a prevalence of parasitaemia detected by mass blood surveys, once a year during the transmission period. The outcome measures were collected 12 months before and 16 months after the impregnation. A bednet fund programme

was introduced in the first year and also evaluated using the baseline incidence rate. The programme significantly increased the availability and use of bednets. These resulted in about 28% effectiveness against malaria incidence and the density of persons/bednet was directly related with malaria incidence ($r = 0.48$, $p<0.05$). In the second year, bans in each pair were randomly allocated either a lambda-cyhalothrin or placebo bednet impregnation. The post-impregnation data showed a small and slow trend of 26% effectiveness. This was not statistically significant. However, the significant effect of 84% reduction was detected amongst adult males after the second impregnation. There was no significant effect on the prevalence of parasitaemia. The sleeping patterns, prevalence of bednet use, dosage and coverage of the impregnation, side-effects and washing rates were also studied. The possible mechanisms of the effect are discussed.

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Chapter 1

Malaria control in Thailand and research questions

1.1 General background

Thailand is a tropical country in the Indo-Chinese peninsula of southeast Asia between 5 to 21 degrees North and 97 to 106 degrees East. The country is bordered by Cambodia and Laos on the east and northeast, by Myanmar on the west and northwest, and by Malaysia on the south (Figure 1.1). Thailand includes tropical rain forests, agriculturally rich plains, and forest-clad hills and mountains. The patterns of rivers and mountains divide Thailand into four natural regions: the mountainous north; the northeast, consisting primarily of the Korat plateau; the central region, consisting primarily of the Chao Phraya Basin; and the south, consisting of the long peninsular extension of Thailand south from the Chao Phraya Basin to the Malaysian frontier. There are 3 seasons in general, hot during February - May, rainy during June - September and cold during October - January. There is more rain in the south and it is colder in the north. The total population was about 57 million in 1990 spread over the area of about 514,000 square kilometres. About 28% of the land area is covered with forest. The major crop is rice.

Administratively, The country is currently divided into 73 provinces, approximately 650 districts, 5,000 townships and 55,000 villages. In socioeconomic terms, Thailand has been experiencing rapid and fundamental social and economic change. The GNP per capita, was $800 in 1985, according to the World Bank, placing it squarely in the middle-range among those developing countries classified as being lower-middle-income. Despite an increasing proportion of the population living in urban areas and engaging in non-agricultural pursuits, the country remains predominately rural and agricultural. According to World Bank statistics, 82 percent of the population lived outside areas classified as urban in 1985 and 71 percent of the labour force was engaged in agriculture in 1980 (World Bank, 1987).

The health service system in Thailand is a complex mixture of public and private providers. In urban areas, private health services are very important. In rural areas, however, the major source of service is the Ministry of Public Health,

operating through an extensive network of outlets including regional health centres, provincial and district hospitals, and local health stations at the township level. The public health system has expanded considerably in the last two decades. For example, the number of government health stations, which are virtually all located in rural areas, more than tripled between 1965 and 1985, at which time there were over 7,000 such stations. In addition, the number of government hospitals more than doubled to over 500 units during the same period, with the increase almost entirely at the district level. In 1985, life expectancy at birth was estimated as 64 years and in 1987, infant mortality rate was estimated as 35 deaths per 1,000 births (Chayovan et al. 1988).

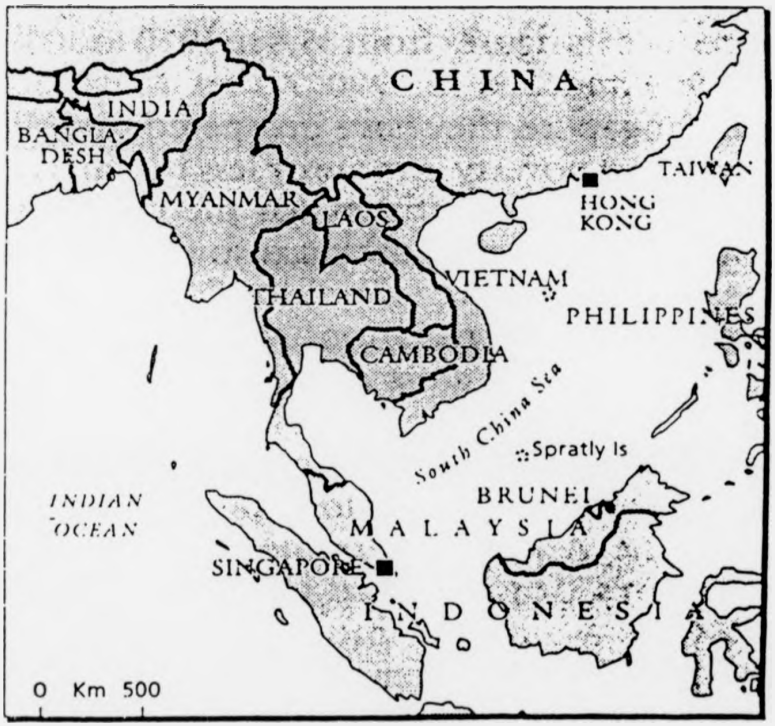


Figure 1.1 Map of Thailand.

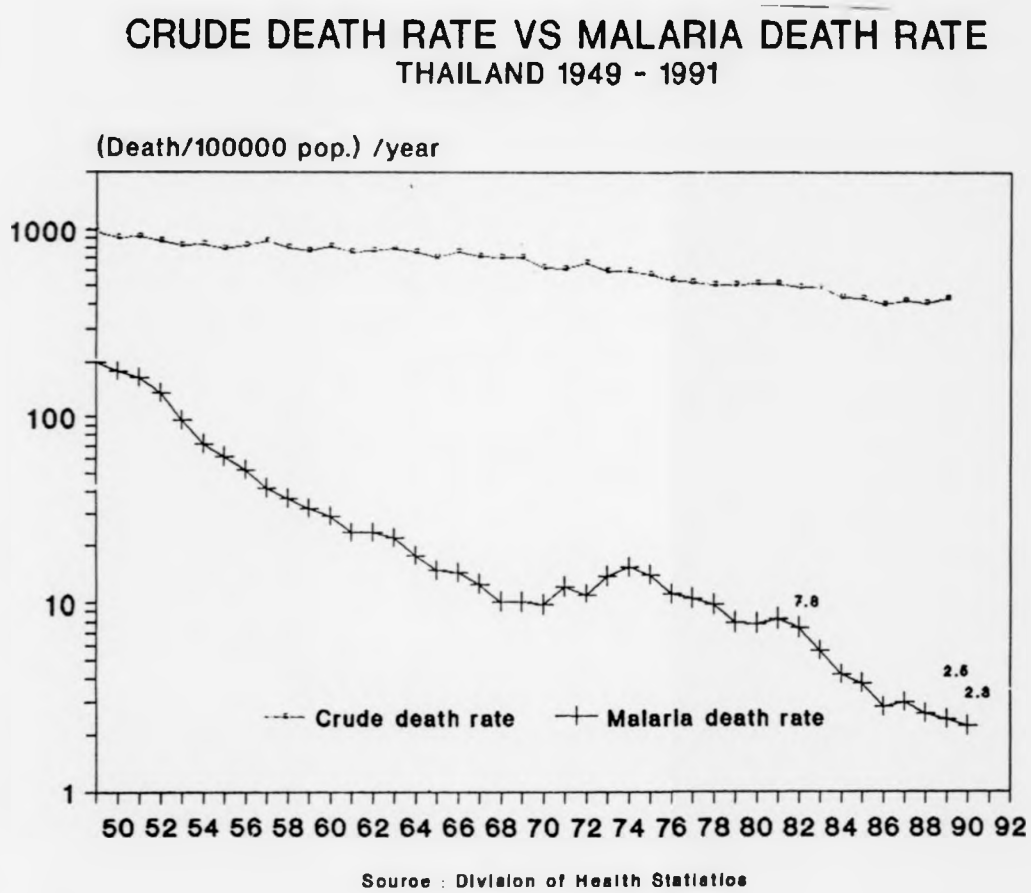
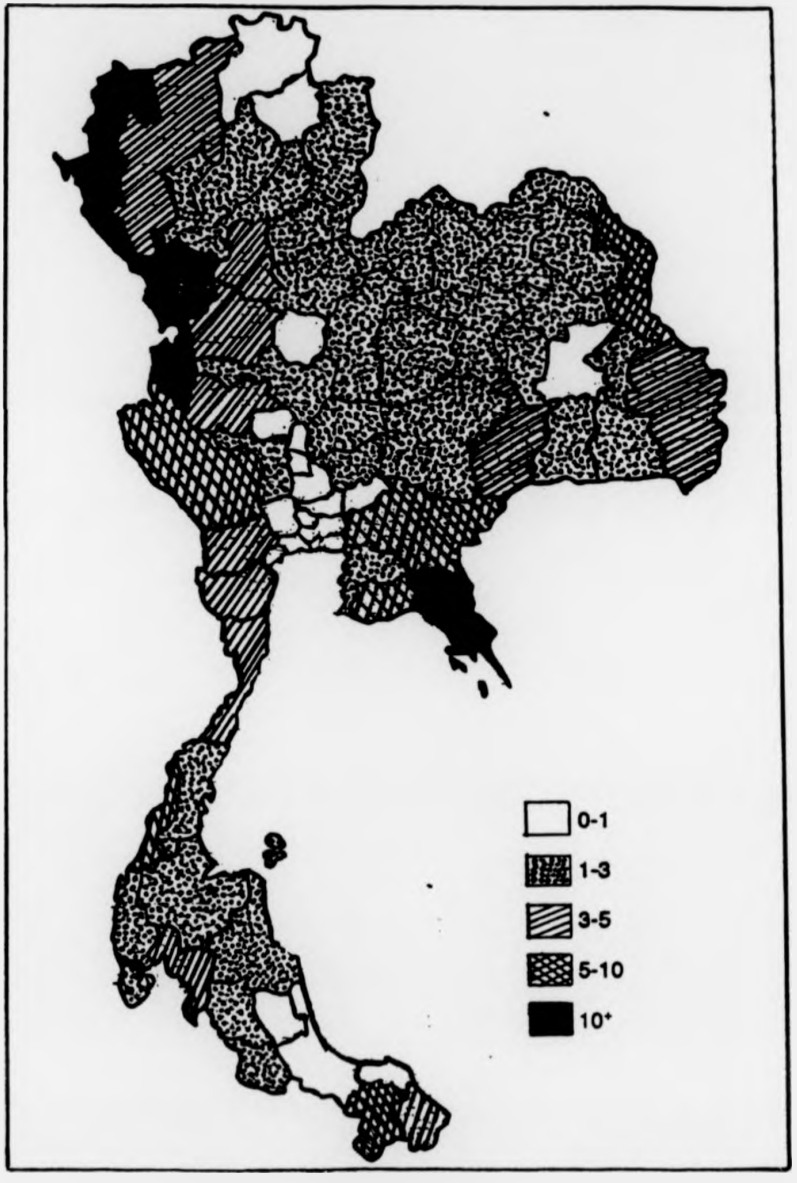


Figure 1.2 Trends of malaria mortality rate in Thailand.

Figure 1.3 Distribution of malaria mortality rate by province.



1.2 Epidemiology of malaria in Thailand

1.2.1 Mortality

Before the DDT spraying operation started, malaria was a leading cause of death with a mortality rate of 328.9 deaths per 100,000 population in 1943 (Ministry of Public Health, 1966). After the operation started in 1949, the death rate has continuously declined to be only 2.3 per 100,000 population in 1990 (Malaria Division, 1991)(Figure 1.2). The mortality rates by province were higher than 10 per 100,000 population among the provinces which border with Myanmar in the northwest and Cambodia in the east (Ketrangsee et al. 1991a) (Figure 1.3).

1.2.2 Morbidity

The incidence of malaria throughout the country has been greatly reduced during the past 35 years. The annual parasite incidence (API) was reduced from 286.0 per 1,000 population in 1947 to 2.2-3.6 in 1966 - 1972. Since then it has risen to 7.1 in 1979 and 10.6 in 1981. The increase is attributed mainly to population movement and parasite resistance to drugs. However, malaria morbidity has shown a downward trend since early 1982 (Figure 1.4) (Ketrangsee et al. 1991a). The reasons for the improvement are not quite clear, but the most plausible reason is the striking increase in the number of malaria clinics and productive malaria volunteers, which has enabled early diagnosis and treatment. There is a small increase in the incidence from 5.0 in 1986 to 5.8 in 1988. This is due to population migration to coffee and rubber plantations in the south. However, it declined to 5.2 in 1990. Figure 1.5 shows the API by province. Again, similar to mortality patterns, the high API provinces are those bordering Myanmar in the west, Cambodia in the east and Malaysia in the south.

Figure 1.4 Trends of malaria morbidity in Thailand.

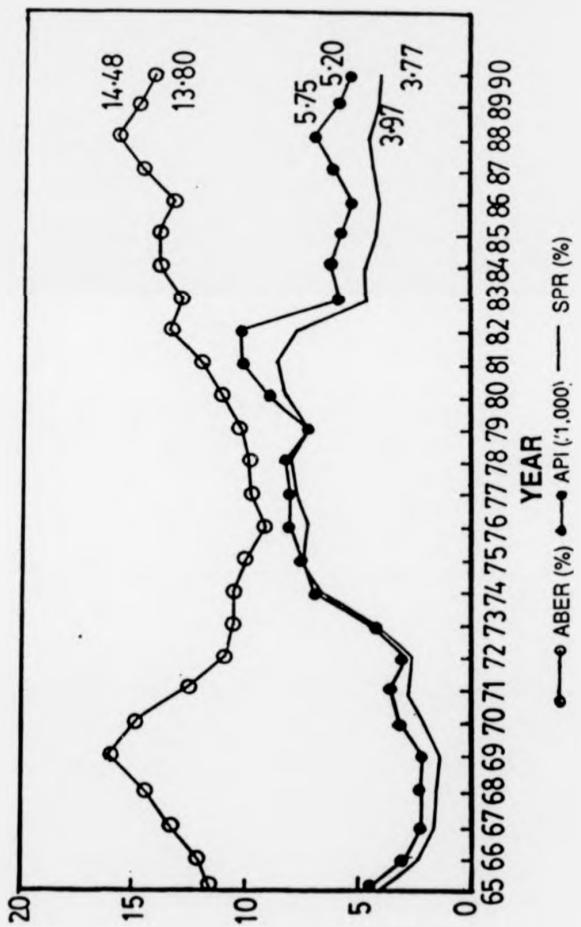
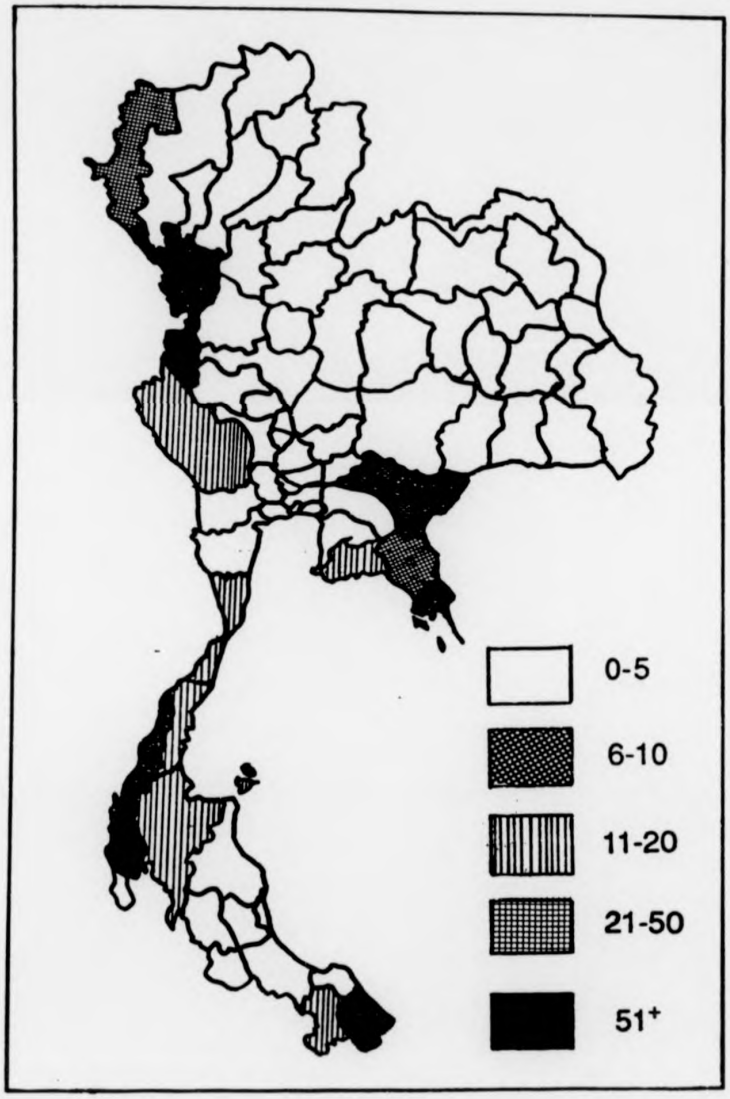


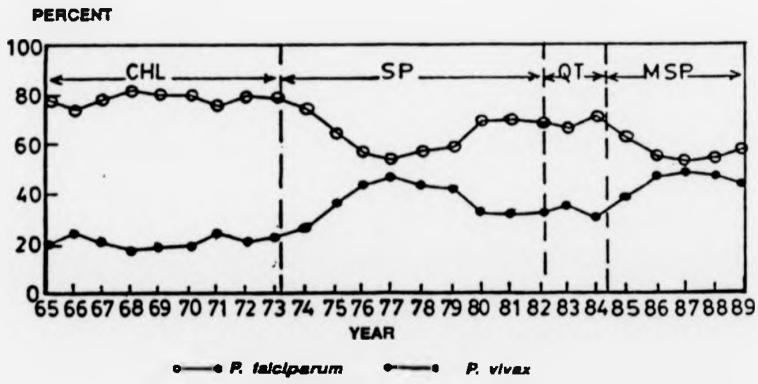
Figure 1.5 Distribution of malaria incidence by province.



1.2.3 Parasitology

The four species of human Plasmodium found in Thailand are P.falciparum, P.vivax, P.malariae and P.ovale. The proportion of P.falciparum was high during the period 1967 - 1974 (70% - 80%) and decreased during 1975 - 1979 (50% - 60%) because of the introduction of sulfadoxine/pyrimethamine in 1973 (Figure 1.6). Then it showed an upward trend during 1980 - 1984 due to the resistance of P.falciparum to sulfadoxine/pyrimethamine and downward trend due to the introduction of mefloquine/sulfadoxine /pyrimethamine (MSP) in 1984 - 1985, to replace sulfadoxine/ pyrimethamine. P.malariae and P.ovale are rare (0.02% and 0.001%, respectively) and scattered only in the northern, southern and border areas (Katrangsee et al. 1991a).

Figure 1.6 Proportion of malaria parasite species and radical drug treatments used, Thailand, 1965 - 1989.



1.2.4 Entomology

The primary vectors in Thailand are Anopheles dirus, An.minimus and An.maculatus. Secondary vectors are An.aconitus and An.sundaicus

An.minimus is present throughout Thailand with the exception of the provinces in the south along the border with Malaysia. An.minimus is most commonly found in slow-moving streams on forested areas, except in the north where it is also found in irrigation canals for rice paddies close to mountains. An.minimus is often found in association with An.maculatus and shares a breeding habitat with that species. Recent studies have suggested that An.minimus is a species complex scattered around the country (Baimai, 1989). An.dirus is found in Thailand primarily in forest areas and plantations. Species A is widespread throughout Thailand except in the south, species B and C are found in the southern peninsula, species D is common along the Thai-Myanmar border in the west, while species F is restricted to the Thai-Malaysian border (Baimai, 1989). In the eastern part, a greater number of An.dirus than An.minimus was found as well as a greater sporozoite infection rate for An.dirus than An.minimus (Prasittisuk et al, 1989).

An.maculatus group is an important vector in the south and the Thai-Malaysia Peninsula where form E is prevalent. Form F and other member species of An.maculatus complex are commonly present throughout central and northern Thailand. Species B and form F are strongly zoophagic and therefore not considered vectors of importance (Upatham et al, 1988). Another member of An.maculatus complex, An.pseudowillmorei, was also found to be a natural malaria vector (Green et al, 1991).

An.aconitus has been implicated as a possible malaria vector through sporozoite studies only once in central Thailand. An.sundaicus plays a role in malaria transmission in marshy areas, coastal areas and islands (Ketrangsee et al, 1991a).

1.3 Malaria control activities

Thailand has gradually developed its medical and public health services since 1888. In 1918, malaria control by quininisation was one of 10 important activities in the Department of Public Health. In 1942, the Department was transformed and expanded to consist of 14 divisions and since then the malaria control programme has been under the responsibility of the Malaria Division. Due to the promising results of DDT residual spraying in Chiang Mai pilot project, a nationwide malaria control programme was initiated in 1951 with active assistance from WHO and U.S. Government (Ministry of Public Health, 1957). The success of this programme led to the adoption of a malaria eradication policy in 1960. The malaria mortality rate fell rapidly from 328.9 in 1943 to 22.8 per 100,000 population in 1963. The technical surveys during 1960 - 1964 indicated that an estimate of over 570,000 lives were saved during 1949 - 1963; and more than 28,000,000 malaria cases prevented. This represented a loss of 370,000 man-years equivalent to about $159,000,000 (Ministry of Public Health, 1966). In 1964, the programme was reorganised to be fully operated as an eradication programme, with an eight year plan of action. The country has been administratively divided into 5 regions. In 1970, the death rate had been further reduced to 10.1 per 100,000 population. However, in 1971, a new policy was developed, as a result of the WHO revised global strategy of malaria eradication, for maintaining the gains already made and for the prevention of the rise of new problem areas. Thus, the plan of operations was revised and implemented for the period 1971 - 1976. This plan was designed to meet the costs of the project in the face of the budget reductions by adjusting programme phasing and developing local criteria for implementation of activities. As a result, the country has been divided into 2 areas, the control and eradication areas. The long term malaria control strategy is operated in the "control area", which is mainly forest and hill areas. The prevention of re-establishment of malaria transmission is performed in the remaining "eradication area" (Prasittisuk, 1985). In 1991, the control area covered about 12.7 million, whereas the eradication area covered about 40.3 million population (Malaria Division, 1991). The eradication area has also been divided into partial and full integration areas, according to the level of the malaria control activities taken up by the general public health services.

1.3.1 Malaria control problems

Although the beneficial impact of residual spraying on malaria transmission has been well-documented, there are major disadvantages. It failed to interrupt transmission in the forest hilly area due to the outdoor behaviour of the two main vectors, An.dirus and An.minimus (Ismail et al, 1975, 1978). The behaviour of An.minimus in this area is different from that found during the beginning of the spraying operation, which was highly indoor biting and resting. This failure resulted in an increase in the spraying refusal rate and caused problems for operations and health education efforts (Prasittisuk, 1985).

Another problem impeding the malaria control effort is resistance of the parasite to antimalarial drugs. It started in 1957 with the resistance of P.falciparum to chloroquine near the Cambodian border (Harinasutta et al, 1962) and gradually spread throughout the country. In 1973, the combination of sulfadoxine and pyrimethamine, as the alternative drug for the treatment of chloroquine resistant falciparum malaria, was introduced into the control programme. However, this led to the development of resistance of the parasite to this combination (Hurwitz et al, 1981), which subsequently became widespread throughout Thailand in 1981 (Pinichpongse et al, 1982). Between 1982 and 1984, a regimen consisting of quinine and tetracyclines was routinely used in Thailand to treat out-patients attending malaria clinics and health institutions with microscopically confirmed falciparum malaria. Owing to compliance problems associated with the 7-day multiple-dose regimen, there was a recrudescence in about 30% of cases. In 1982, type II resistance to mefloquine was reported (Boudreau et al, 1982). However, after a large-scale trial, the triple combination of mefloquine/sulfadoxine/pyrimethamine (Fansimef^{R}) was introduced in 1985 on a strict country-wide operation as a radical treatment of all microscopically confirmed falciparum cases. In early 1985 the Malaria Programme conducted studies to determine the continued efficacy of Fansimef^{R} in the treatment of falciparum malaria in five representative areas. By 1989, the cure rate decreased to 55% in the eastern provinces (Rooney & Thimasarn, 1991). In 1991, the low cure rate was also found on the Thai-Myanmar border (Nosten et al, 1991) and a report of cross-resistance to halofantrine made the situation worse (Ketrangsee et al, 1991b).

The last but not least important problem is population migration and

movement, both within and across the borders (Ketrangsee et al. 1991a). Occupational migration of Thai people to the Cambodian border area for gem mining, and local migration from villages to forests for cutting timber and expanded cultivation in foothill forest areas have resulted in an increase of malaria transmission (Sommani et al. 1983; Butraporn et al. 1986; Singhanetra-Renard, 1986). In addition, mass influx of refugees across the border during the political conflict has also led to an increase of malaria cases in border areas (Meek, 1988). These have all led to the spread of multi-drug resistant falciparum, both within and outside of the country.

1.3.2 Present measures

In the control area, DDT spraying operations and active case detection activity have still been carried out regularly by malaria workers, while it has been stopped in the eradication area. Passive case detections operate in all areas. The principal techniques, employed to overcome the problem of the exophilic behaviour of the vector, are the use of larvivorous fish, thermal fogging with Fenitrothion in epidemic situations and encouraging the use of personal protection measures, such as mosquitoes nets and repellents, through health education activity (Malikul, 1987). Fansidar^{R} and primaquine are used as the presumptive drug. Fansimef^{R} is still the first drug of choice for falciparum malaria.

Details of the main control measures are as follows (Ketrangsee et al. 1991):

1. Residual insecticide house indoor spraying with DDT at 2 gm/m^2 or Fenitrothion at 1 gm/m^2 once or twice a year, covering about 2.2 million population

2. Case detection and treatment through active case detection by malaria clinics, health centres and village malaria volunteers. Presumptive treatment using 2 tablets of sulfadoxine and pyrimethamine together with 30 mg primaquine is generally administered. A triple combination of mefloquine/sulfadoxine/ pyrimethamine (MSP-3 tablets) together with 30 mg primaquine is given as a single dose for radical treatment of Plasmodium falciparum cases. In cases of treatment failure or contraindications to MSP, quinine (7-day course) or quinine (3 days) and tetracyclines (7 days) plus 30 mg primaquine are the alternative regimens. Chloroquine 1500 mg base over a 3-day period with 15 mg primaquine for 14 days is given to patients with P.vivax or P.malariae or even P.ovale

3. Health education is considered a major malaria control measure at all levels. All kinds and means of health education have been introduced at the village and community levels to encourage villagers and communities to become involved in the control and prevention of malaria. In 1989, there were 38,787 malaria volunteers (in 31,650 villages) acting as case finding agents for malaria at the village level. Use of personal protection measures, e.g. mosquito nets, coils or repellents, is also encouraged. Supplementary measures such as space spraying and use of larvivorous fish were also adopted.

1.4 Future plan

Operational strategies for the Anti-Malaria Programme in the future will basically continue to be the same as previously mentioned. However, further development of new technologies will be incorporated, including new methods of insecticide application. These are required to simplify and facilitate use by the community, avoiding have to use complicated equipment. A close relationship between research institutes and the Anti-Malaria Programme will be encouraged to develop capability for solving operational problems, especially in forests and to deal with forest related malaria. Research on the following topics are encouraged (Ketrangsee et al. 1991a).

1. Dynamics of malaria transmission in southern, western and northern Thailand.

2. Epidemiology of drug resistance in Thailand.

3. Field trials with alternative vector control measures such as insecticide-impregnated bednets, mosquitoes coils, repellents and new alternative insecticides such as deltamethrin, lambda-cyhalothrin and ethopenfox.

4. Impact of ecological changes on malaria transmission from cleared foothill areas to rubber plantation and fruit orchards in eastern Thailand.

5. Early warning system, using the existing parasitological, entomological and epidemiological information, to predict malaria outbreaks in low malarious areas.

6. Field-testing of new diagnostic methods of DNA probes.

7. Seroepidemiology to determine malaria endemicity in different ecological settings.

8. Sociological study in relation to malaria infection and control among different groups of people in forest areas.

9. Malaria control approaches among migrant population groups, especially gem-miners.

10. Impact of DDT spraying on malaria control operations in different epidemiological situations.

1.5 Research questions

This thesis describes details of studies following the 3rd topic, on the field trials of a community-wide control programme with lambda-cyhalothrin impregnated bed nets in the forest area of Mae Hong Son province; and the 8th topic, on the sociological aspects of villager movements and malaria illness.

1.5.1 How did a villager in the forest border area of Northwestern Thailand get a malaria illness ?

1.5.2 Can a community-wide programme of a lambda-cyhalothrin bednet impregnation reduce the malaria morbidity in this area ?

Chapter 2

Study area : Mae Sariang District, Mae Hong Son.

2.1 Rationale for the study area

The study in this thesis was to follow the guidelinesof the Individual Training Grant received from the Special Programme for Research and Training in Tropical Diseases (TDR) under the framework of the Institute Strengthening Grant given to Chiang Mai University, Thailand. This was aimed at strengthening research abilities in the field needed for improving the prevention and control of six TDR-targeted tropical diseases, including malaria, in Northern Thailand.

2.2 Northern Thailand.

Most of the areas in this region are mountainous with many types of forest covering about 47% of the total area. It has the second poorest socioeconomic status in the country, after the northeast region. There are limited fertile lowland areas for growing agricultural crops. Large numbers of the rural population have to earn their living from growing upland crops, trading or becoming farm/non-farm wage workers (Singhanetra-Renard, 1986). The control of malaria in northern Thailand is under the responsibility of the Malaria Centre of Region II in Chiang Mai, covering 8,053,613 population in 13 provinces in the North (Malaria Division, 1991).

2.2.1 Mortality and morbidity

In 1949, before DDT spraying, a survey in Chiang Mai found about a 90% spleen rate. This sharply declined to only 1% in 1959 (WHO/SEA, 1960). In 1987, the malaria mortality was 3.1 per 100,000 population (Table 2.1). It decreased to 2.1 in 1990. The annual parasite incidence (API) was 3.65 in 1986, increased to 3.84 in 1987, decreased to 3.20, 2.74 and 2.64 in 1988,1989 and 1990 respectively. The high malaria mortality and morbidity in the region have been confined to the border areas with Myanmar (Figure 1.3 and 1.5).

2.2.2 Parasitology

About 58% of cases were falciparum malaria in 1986. This increased to 67% in 1990. P.vivax, P.malariae and mixed infections were 32%, 0.1% and 0.8% respectively in 1990 (Malaria Division, 1991).

Table 2.1 Malaria mortality and morbidity in the north, 1986-1990.

	Population	Bl.exam.	Cases	%ABER	%SPR	API	M.R.
1986	7,766,446	2,150,944	28,379	27.7	1.32	3.7	n.a.
1987	7,890,780	2,479,127	30,279	31.4	1.22	3.8	3.1
1988	7,958,830	2,478,471	25,473	31.1	1.03	3.2	2.6
1989	8,035,211	2,359,777	21,998	29.4	0.93	2.7	2.1
1990	8,122,274	2,253,861	21,455	27.8	0.95	2.6	2.1

%ABER - Annual blood examination rate (%)
%SPR - Slide positive rate (%)
API - Annual parasite rate (cases/1,000 persons/year)
M.R. - Mortality rate (deaths/100,000 population/year)

2.2.3 Entomology

Before starting DDT spraying, the major vectors in the north were found to be an endophilic and endophagic An.minimus (Ministry of Public Health, 1957). In 1959, an independent appraisal team from WHO came to evaluate the situation at Chiang Mai province in the north. They reported the satisfactory eradication of An.minimus in the plain areas by DDT spraying (WHO/SEA, 1960). However, they found transmission still occurring in the hill villages and explained this by the number of An.minimus and An.dirus (known as An.balabacensis then) found. Later, the role of An.dirus, in malaria transmission in forested areas, was confirmed in eastern Thailand (Scanlon and Sandhinand, 1965).

In the forest and forested fringe areas of Pitsanulok province, northern Thailand, Ismail et al (1974, 1975, 1978) reported the effects of DDT spraying on malaria transmission. They found that transmission was perennial. An.dirus was maintaining transmission all the year round inside the deep forest; and

only in the monsoon season in the forest fringe and its surrounding area. An.minimus was maintaining transmission during the dry season, late in the year, and appeared to be more exophagic than An.dirus, but both seemed to be exophilic. The vectorial capacity of, as well as the impact of DDT spraying on, An.dirus was higher than that of An.minimus. DDT spraying alone, though it had a considerable effect on the reduction of the vectorial capacity of the vectors, was not enough to interrupt transmission in the area. After DDT spraying, both vectors bit earlier, especially An.minimus during the dry season, and more outdoors than before the spraying. Forest clearance seemed to lead to the disappearance of An.dirus and favoured the prevalence of An.minimus. With the development of cleared areas in the foothills, An.minimus alone was expected to maintain transmission, though at a much lower level.

However, 10 years later, Baimai et al (1988) reported the geographical distribution of the An.dirus complex in Thailand. It was noticed that the vector varied both in numbers and types of species throughout the country. In the north, the prevalence of An.dirus along the Thai-Myanmar border were less than those areas eastward. This confirmed the finding by Harbach et al, in 1987, reporting the predominance of An.minimus and the scarcity of An.dirus in the mountain of Tak province, close to Thai-Myanmar border. An.maculatus was also common but no sporozoites were found in it. They concluded that An.minimus may be the major vector in the area.

2.2.4 Sociological aspects

Population movements were common in the north, both within and across the forest border areas (Singhanetra-Renard, 1986). These are due to socioeconomic reasons and political conflicts. Villagers in the area are used to moving into the forest hilly areas for growing upland crops. Many socioeconomic development projects in the area also cause a high level of labour movements, from both within the country and abroad, into the area. When there is fighting along the Thai-Myanmar border between ethnic minorities and the Myanmar government, many refugees flee into Thai territory.

These movements have resulted in a high malaria incidence, due to three main factors.

1) The exposure of immigrants to malaria vectors in forested areas, especially at night.

2) Contact between infected Burmese, Karen or Shan from across the border with uninfected, non- or semi-immune people inside Thailand.

3) Control measures designed for the general population are not effective among highly mobile populations engaging in illegal activities.

As described above, the malaria problems in the north are located at Mae Hong Son province close to Thai-Myanmar border. Hence, the southern part of the province, i.e. Mae Sariang district and Sob Moey subdistrict, were chosen for the studies. Below are some details of Mae Hong Son province and the study area.

2.3 Mae Hong Son province

The province is situated between 17 - 20 degrees north and 97 - 99 degrees east. It had about 167,000 population in 1990, spread over the total 13,184 square kilometres of forest hilly areas. Only about 1% of the area is used for agricultural purposes. The main crop is rice. There are 5 districts and 1 subdistrict, spread along the Thai-Myanmar border. It borders with Myanmar in the north and west, with Chiang Mai province in the east and with Tak province in the south (Figure 2.1). There are flights from Chiang Mai or Bangkok to Mae Hong Son and back everyday. Apart from this, the way to reach the province is by road, from Chiang Mai and Tak province. It is about 400 and 900 kilometres from Chiang Mai and Bangkok respectively. Before 1991, there was only one road from Chiang Mai to the main town of Mae Hong Son. It takes about 8-9 hours, passing through the Mae Sariang district in the south of the province. Since 1991, a new road from Chiang Mai, passing through the north of the province, has been completed, and it takes about 5 hours travelling time. The altitude of the main towns is about 211 - 267 metres above the sea level. Most of the people in this province are of the Karen ethnic minority. Their socioeconomic status is poor, although the area is rich in mineral deposits of wolfram, manganese, fluorite and tin, as well as forest products.

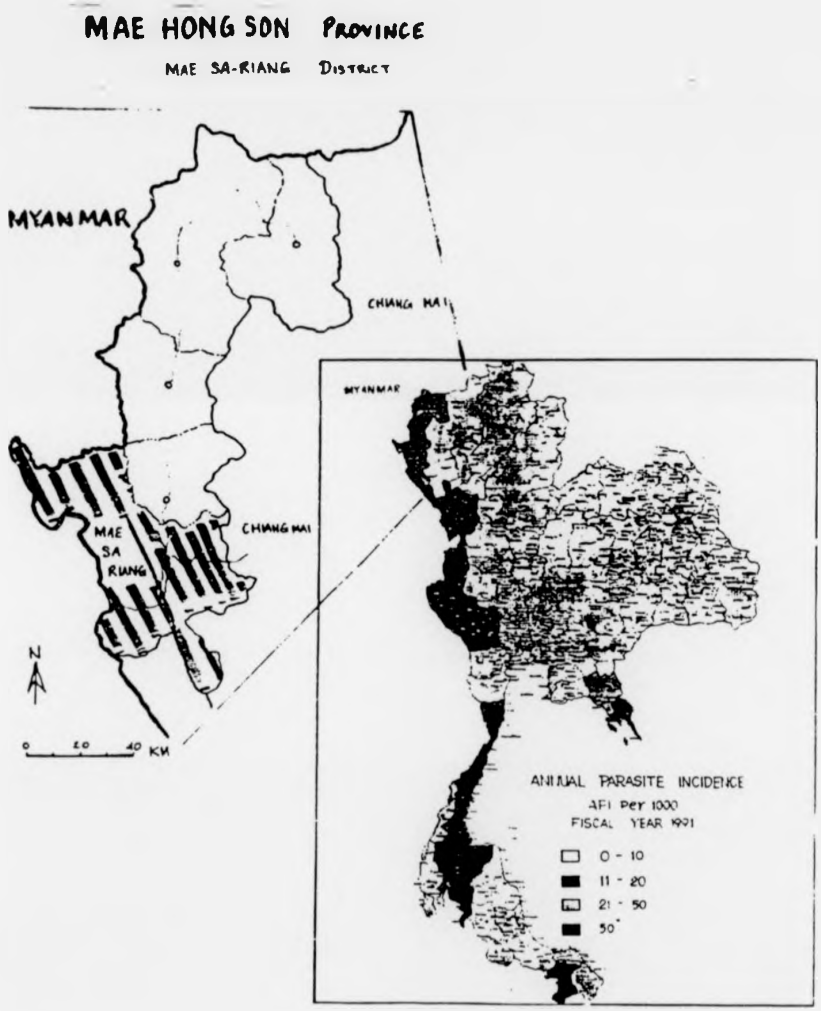


Figure 2.1 Map of Mae Sariang District.

2.3.1 Malaria and its control

The annual parasite incidence (API) in Mae Hong Son has increased from 30 per 1,000 persons in 1986 to 53.7, 47.2 and 52.7 between 1987 - 1989. This is about 18 - 19 times higher than the rest of region II (Table 2.2).

Table 2.2 Malaria mortality and morbidity in Mae Hong Son, 1986-1990.

	Population	Bl.exam.	Cases	%ABER	%SPR	API	M.R.
1986							
Mae Hong Son	154,473	180,077	4,640	116.6	2.58	30.0	
Others	7,611,973	1,970,867	23,739	25.9	1.20	3.1	
Total	7,766,446	2,150,944	28,379	27.7	1.32	3.7	
1987							
Mae Hong Son	158,733	271,608	8,528	171.1	3.14	53.7	17.0
Others	7,732,047	2,207,519	21,751	28.6	0.99	2.8	2.8
Total	7,890,780	2,479,127	30,279	31.4	1.22	3.8	3.1
1988							
Mae Hong Son	158,922	254,436	7,501	160.1	2.95	47.2	12.0
Others	7,799,908	2,224,035	17,972	28.5	0.81	2.3	2.0
Total	7,958,830	2,478,471	25,473	31.1	1.03	3.2	2.6
1989							
Mae Hong Son	161,087	287,087	8,491	178.2	2.96	52.7	6.8
Others	7,874,124	2,072,690	13,507	26.3	0.65	1.7	2.0
Total	8,035,211	2,359,777	21,998	29.4	0.93	2.7	2.1
1990							
Mae Hong Son	166,050	269,880	7,938	162.5	2.94	47.8	13.2
Others	7,956,224	1,983,981	13,517	24.9	0.68	1.7	1.9
Total	8,122,274	2,253,861	21,455	27.8	0.95	2.6	2.1

%ABER - Annual blood examination rate (%)
%SPR - Slide positive rate (%)
API - Annual parasite incidence (cases/1,000 persons/year)
M.R. - Mortality rate (deaths/100,000 population/year)

Resources in the Regional Malaria Centre II have been mobilised to solve the problem in this province. Apart from routine control activities, with DDT spraying, larvivorous fish, health education, early case detection and treatment, additional efforts have been put in to increase the activities of the case detection system, aimed at preventing an outbreak of the disease. The annual blood examination rates were raised up to about 160 - 170% (Table 2.1), which were about 6 times higher than those in the rest of the region. However, the situation has not been satisfactorily controlled. These difficulties have also been experienced along Thai-Myanmar border, from Mae Hong Son in Region II down to Tak, Kanchanaburi and Ranong in other Regions (Sornmani et al, 1983, Ketrangsee et al, 1991). Hence, there is an emergency need for finding new ways to alleviate the problem along these areas.

2.3.2 Mae Sariang district

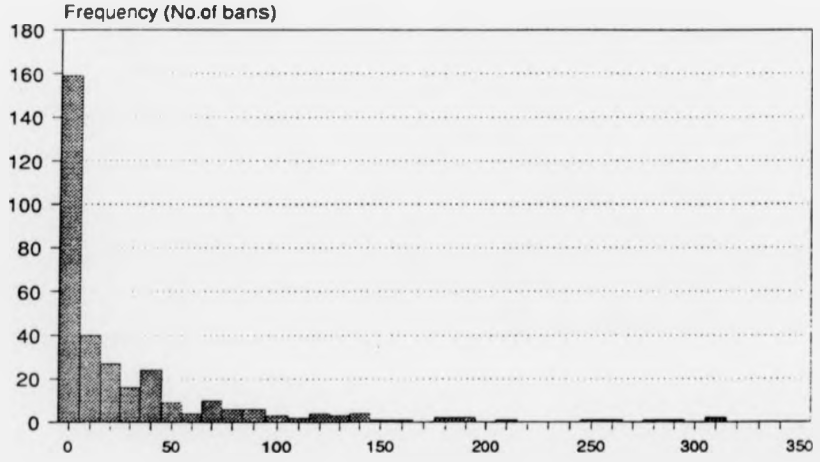
Mae Sariang district used to be the biggest district in Mae Hong Son province, consisting of about 40% of the total population of Mae Hong Son. Recently, Sob Moey subdistrict was partially separated from the district, taking with it about one third of the district's population. However, it was also included in the studies. Hence, for convenience, both will be called Mae Sariang district throughout this thesis.

The district is the south end of Mae Hong Son province. It borders with Mae La Noi district in the north, Chiang Mai province in the east, Tak province in the south and Myanmar in the west (Figure 2.1). The altitude is 211 meters above sea level. The amount of rain in 1989 was 788.7 millimetres. In 1989, the district had 61,099 population, spread over 4,555 square kilometres. The majority are of the Karen ethnic minority. The Karen has 2 subgroups, Skaw and Pkow. In Mae Sariang, the majority is the Skaw with a few Pkow near Tak province in the south. Both speak differently from each other and from Thai. The local Thais in the district are a mixture of Shan and northmost Thai over many generations. They can use both local and official Thai. The only way to gain access to the district is by a road from Chiang Mai. It has also been the only gateway to the main town of Mae Hong Son before 1991. It is about 200 kilometres, or 4 hours, from Chiang Mai by a hilly road. From the geographical setting, Mae Sariang has always benefitted most from the

socioeconomic development activities which flow into the province. It is also the route of both legal and illegal business between Thailand and Myanmar. This explains why it is the biggest district in the province in terms of both population and socioeconomic status.

Administratively, the district consists of 13 cantons, 109 villages and 305 household groups. **A household group is the smallest community unit in malaria control administration. It is called a "ban" in Thai. For convenience, it will be called a "ban" throughout this thesis.** These bans are covered by 2 malaria sectors with about 15 fulltime malaria workers together. Analysis of the routine data, from October 1988 to September 1989, revealed that there were 1,610 cases, and the annual parasite incidence (API) in the district was 26.4 per 1,000 persons. When analyzing the data by ban, the incidence rates varied from 0 - 313 per 1,000 persons. Ninety four (31%) and 56 (18%) bans have a rate of more than 30 and 50 per 1,000 persons respectively. Figure 2.2 shows the distribution of the incidence rate (API) by household group. This formed the basis for calculating sample sizes in the study on the effectiveness of the bed net impregnation programme.

Figure 2.2 The annual parasite incidence (API) in Mae Sariang district, by ban



Chapter 3

Villager movements and Malaria illness

3.1 Background information and research questions

3.1.1 Population movements and malaria

Studies on population have 3 components; mortality, fertility and migration; however, it is more difficult to measure a migration than a birth or death. The term migration was used in the past to describe population movement. Censuses and most large-scale surveys can capture only a small part of the population movement. It is more dynamic and has many intricate dimensions, e.g. spatial, temporal, residence, and activity (Standing, 1984). In general, movements may be classified into two main types; migration, movement involving change of residence; and circulation, movement away from place of residence, but eventual return to it (Prothero, 1977; Skeldon, 1990). Its determinants and consequences can be socio-economic factors (Oberai & Bilsborrow, 1984; Skeldon, 1990), as well as health hazard (Bruce-Chwatt, 1968; Prothero, 1977).

Population movements of various types have long been recognised as a factor causing high malaria incidence. Ross (1911) mentioned examples of cases related to movements. He defined them as either imported cases, when the infected person immigrates into the locality; or extraneous infected cases, where persons from a locality of low endemicity get infected during occasional visits to a highly endemic locality, outside their usual habitation. He also mentioned the need to do quantitative studies of the relationship of movement and malaria incidence. In Africa, Walton (1947) found that the entomological data collected in Freetown, Sierra Leone, could not totally explain a higher observed than expected rate of malaria infections in young children. He suggested that the majority of these infections were contracted from sources located outside the city. During the period of the global malaria eradication campaign, WHO (1957) considered this a special problem that could have serious impact on the success of the eradication programme. Prothero (1961, 1965) reported in an extensive geographical study that population movements are a problem of

malaria eradication in Africa. Movement is common both within and across country boundaries, relating to traditional, political and socioeconomic patterns. It constitutes a serious problem by increasing the spread of the disease and obstructing control measures.

In Brazil, malaria incidence has increased more than 70% since 1970 (Sawyer, 1986). This has been due to many colonization projects, rural settlements and migrations into the tropical rain forest areas. In India, various development activities, human behaviour related both to man-vector contact and malaria control measures , and population movements have been complex obstacles to malaria control (Reuben, 1989). A study on the fishing population on Rameswaram Island suggested the relationship between seasonal circular movements and the geographical distribution of malaria incidence (Rajagopalan et al. 1986). Lack of appreciation of this factor has led to considerable waste of effort in applying vector-control measures in the wrong place. In Singapore, many outbreaks have occurred since 1964 (Goh, 1986). The rapid urbanisation and industrialisation programmes disrupted the existing comprehensive anti-malarial drainage system which had been in operation for more than 50 years. The close social, cultural and economic interaction between the islanders and their neighbours in the border areas, the free population movement across the borders with Malaysia and Indonesia, and the irregular vector control services resulted in a continual transmission of malaria in these islands.

Based on the African experience, Prothero (1977) proposed a space-time typology of mobility. He divided migration into 2 categories; regular and irregular migration. Circulation is divided into 4 categories: 'daily' (away from place of residence for up to 24 hours); 'periodic' (away for more than 24 hours but less than 12 months); 'seasonal' (a special category of periodic where the time absent is related to the span of one or more seasons); and 'long-term' (away for more than 12 months and possibly extending over years). In each category, mobility can be classified into 4 types by places of residence and destination; rural-rural, rural-urban, urban-rural and urban-urban.

Different activities of people can be associated with the different categories of circulation and migration and, in turn, can be associated with categories of health hazards. Firstly, movement from one set of ecological conditions to another

can result in an exposure to vectors of many diseases. Secondly, movements bring different groups of people into contact with one another and the possibility of transmission of disease. Thirdly, physical and psychological stress may result from movement because of biomedical and socioeconomic pressures in adjusting to new environments. Further quantitative geographical analysis was suggested.

Ault (1989), in his extensive review, described population movements, related to the geographic spread of malaria, in 8 general forms.

1. One-way migration to seek economic opportunity (e.g., agricultural settlers);

2. Circular migrations on a seasonal/annual cycle (e.g., pastoral nomads or seasonal agricultural labourers);

3. Regional trade and marketing movements;

4. Tourism, either local or international;

5. Pilgrimages (e.g., Muslims to Mecca);

6. Movement for medical treatment;

7. Spontaneous involuntary migration in response to war or natural disasters;

8. Returning military personnel.

Kondrashin and Orlov (1989) suggested many practical implications of population movement on malaria. The constant two-way movement of people between the transmission areas and the malaria-free areas can cause outbreaks and result in re-establishing malaria endemicity in the latter. The continuous flood of non-immune migrant labourers into gem-mining areas on the Thai-Cambodia border can result in the spread of drug-resistant malaria to the north, northeast and northwest of Thailand, as well as Myanmar and Sri Lanka. The rural-urban movement, following rapid industrialisation, can maintain transmission in the urban areas in India. Movement can result in changing patterns of malaria epidemiology, according to geographical area, age, sex, occupation, tourists, pilgrims, transport workers, military personnel and refugees. Mortality among imported cases is high and vectors can also be introduced through population movement.

3.1.2 Population movements and malaria in Thailand

In Thailand, various types and amounts of movement occur at both international and inter-country levels. Circular movements of villagers into and from the forest hilly areas have long been mentioned to be the common human factor impeding the progress of malaria control in the north (WHO/SEA, 1960, Ismail et al. 1974). During the 1970s, about half a million Cambodian refugees fled into Thailand. Many of them were infected with P.falciparum parasites that did not respond to sulfadoxine-pyrimethamine combination (Harinasuta et al. 1982). Research was encouraged on the socio-economic aspects of malaria and its control with particular reference to population movement patterns, human behaviour and attitudes, and agricultural practice in relation to the transmission season. Sommani et al (1983) using structured questionnaires, in-depth interviews, and participant observation, reported patterns of temporary migrant labours and their malaria experiences in Bo Ploi district, Kanchanaburi Province. Kanjanapan (1983) further reported the higher prevalence of malaria in this group compared to the local people. Many studies also described various epidemiological and entomological situations in displaced persons, both at the eastern border with Cambodia (Meek, 1988) and western border with Myanmar (Shanks et al, 1990; Decludt et al. 1991) with no systematic attempt to relate them with movements. Butraporn et al (1986) used a matched case-control design to study social, behavioral, and housing risk factors in the east. He reported a high risk of getting malaria in houses situated near the forest, having movements into the forest, irregular use of bed nets, poor housing conditions and living with a malaria patient. There were no quantitative details on the types of movement reported. The case-control study by Fungladda et al (1987) also revealed a 7.19 and 10.25 higher malaria risk of working and residing in forested areas in the west.

In the North, an extensive geographic study, using field observations and in-depth interviews, by Singhanetra-Renard (1986) pointed out details of movements in the areas with a high incidence of malaria. Those places were classified into 2 kinds of settlements, the remote upland forested and border areas. In the first kind of settlement, the villagers are located off the main road, in a remote and forested area. They have very few rice fields and cannot grow enough rice to meet household consumption needs. They are, therefore, forced to make their living

by engaging in various other economic activities, resulting in very complex movements. Although some may go to sell their labour in urban areas in the country or overseas, most of them are engaged in more traditional activities like swiddening, logging and hunting, which leads them into forested areas.

In border settlements, the problem is far more serious. There has long been political conflict between the Myanmar government and ethnic minorities along the border with Thailand, including the Karen which belong to the Karen National Defense Organisation. There are no malaria control services in the Myanmar side of the area since they are beyond the reach of Myanmar and Thai governments. This allows traders and labourers uncontrollable access to cross the area regularly. There are many socioeconomic development projects in the area, such as forest and mining industries, the construction of roads and irrigation schemes, as well as the development of plantations. In these projects, many workers from across the border are hired for a low wage, which they willingly accept.

Singhanetra-Renard (1986) also suggested the relationship between the transmission of malaria and movement for various illegal economic activities. These include logging, game poaching in national forests and parks, smuggling of cattle and goods, and crossing the border illegally. Such activities have resulted in a high rate of incidence of malaria among the movers. This is suggested to be due to three main factors:

1. The exposure of movers to malaria vectors in forested areas especially at night, due to the nature of their activities.

2. Contact between infected Burmese, Karen, Shan, or Laotians from across the border with uninfected, non-immune people inside Thailand.

3. Control measures designed for the general population are not effective among highly mobile populations engaging in illegal activities since they are very reluctant to reveal anything about their activities and when or where they carried them out.

These excellent qualitative findings lay a foundation for further quantitative studies to enable the control programme to set priorities and effectively plan for resources allocation.

In Mae Hong Son province, there were 7,938 malaria cases among the local people during October 1989 to September 1990. About 34% and 18% of those cases were reportedly contracted, respectively, locally in the forest and abroad in Myanmar (Ketrangsee et al, 1991a). These are findings from routine investigations among the cases. To show the real relationship between these movements and risks of malaria illness, a simultaneous investigation among healthy people is needed. In this study, the quantity of exposure of villagers engaged in various circular movements were studied, and related to the risks of getting malaria illness.

3.1.3 Methodological issues and research questions

In general, there are three possible levels of study in terms of depth of subject matter covered. These may be conceptualised in terms of their primary purpose : (1) to *measure* rates of movement, (2) to *describe* the movement, and (3) to *explain* the movement, its causes and consequences (Bilsborrow, 1984). A study aimed at the latter level should be able to compare the determinants or consequences in two ways; between movers and non-movers, and between before and after movement. The useful measure of the extent of circulation should consist of the number of movers, the duration, total period of observation and population at risk (Standing, 1984). This is very useful for analytical purposes. To adapt these concepts to study circular movement in this area, estimates have to be made of the size and patterns of movement, and correlated with the consequence of malaria illness.

Population census is traditionally used to estimate the size of movement but short-term and short-distance movements tended to be underestimated. Specialized surveys, retrospectively explore lifetime mobility and yield more details with the difficulties of recall (Bilsborrow, 1984; Skeldon, 1990). Although, this may be alleviated by the use of the life-history matrix (Balan et al, 1969), the results can still be weakened by the recall problem,especially the time boundary. The best way to get unbiased, reliable and rich data is a longitudinal or series of repeated studies at a household level. This can capture all forms of short-term mobility or circulation (Chapman and Prothero, 1983; Bilsborrow, 1984; Skeldon, 1990). Singhanetra-Renard (1981) used a longitudinal mobility register to study mobility in Northern Thailand and reported that 96% of all movements had durations of only 6-24 hours. This also enabled her to analyze the movements in terms of space and time. This method is

used here to describe the size and patterns of villager circular movements, in terms of both persons and person-times, and their empirical relationship to malaria illness.

This study has 3 objectives:

1. To measure the size and describe villager circular movements that occur overnight.

2. To measure the risks of getting malaria illness from those movements.

3. To measure the effects of a bed net on those risks.

3.2 Materials and Methods

3.2.1 Study area :

The smallest unit considered by the malaria control programme in Thailand is called a 'ban'. Five bans in Mae Sariang district, with an annual parasite incidence (API) higher than 50 per 1,000 persons/year, were included in this study. These were also the bans included in the entomological study during 1990 - 1991 by another entomological team. One of them is located in a deep valley in forested hills, and is accessible with difficulty, especially during the rainy season. Two of them are located in the lower forested hilly areas and the others are located in a forested plain area. They are about 0.8 - 30 kilometres apart and accessible throughout the year by at least a motorcycle. In 1989, the total population was 1259, and ranged from 90 to 719 persons per ban. All inhabitants are Karen. Many of them can read and speak Thai but communication is always better in the Karen language.

From the initial census survey, it was found that about 50 % of households in the study bans already possessed one or more nets. About 90 % of these nets were made from cotton or poly-cotton (a netting material with cotton and polyethylene threads interwoven). Two of the 5 bans received more nets through their bednet fund in May 1990. The others received more nets in February 1991.

3.2.2 Study design :

This study was a small cohort study designed as a substudy of a larger impregnated bednet intervention study in the district (see the next chapter). DDT spraying in these bans had been stopped since October 1989. The study was carried out during 15 months of the transmission period, from 1 July 1990 to 20 February

1991 and 1 June 1991 to 20 February 1992.

3.2.3 Outcome measures :

1. Proportion of movement
2. Incidence of malaria illness

3.2.4 Sample size and sampling :

The second outcome measure in terms of the relative risk of movement was used as a basis for calculating the sample size. Analysis of the data collected by a routine investigation of malaria workers in Mae Sariang district in 1989, showed that more than 95% of malaria cases had gone out of their houses. However, this cannot be directly attributable to movements because a considerable proportion of movers may also be healthy. Butraporn et al (1986) reported malaria relative risks (odds ratios) of moving into the forest of 5.2 and 14.3 for occasional and frequent movements, in the eastern part of Thailand. Their table was recalculated and the overall relative risk (odds ratio) for movement was 8.5 (95% confidence interval are 5.5-13.2). Sornmani et al (1983) reported about 40% of local people in Kan-chanaburi province, western Thailand, were housewives and children, who might not be involved in any movements. About 66% of migrants in the area stayed less than 6 months at any one time. Later in the same province, Fungladda et al (1987) reported 7.19 (4.41-11.73) and 10.25 (6.28-16.74) higher malaria risks for working and residing in forested area.

It is, therefore, assumed that about two third of villagers in this area are movers and they would have about 8.5 times higher risk of contracting malaria than non-movers. The overall incidence rate of the study bans in 1989 was 130.3 episodes per 1,000 person-years, respectively. The expected incidence rate for non-movers is estimated to be about 20/1,000 person-years. Based on these estimates, the sample size required for detecting such risk of movement, with 95% precision and 90% power, is 210 person-years (using Epi Info software programme, in which Fleiss, "statistical Methods for Rates and Proportions", 2nd Ed., Wiley, 1981, 38-45, was quoted). However, only movements during the high transmission period were considered interesting and limited resources permitted analysis. Therefore, the sample size was increased to 360 persons, or about 30% of the total population, followed up for 7 months, from July 1990 to January 1991. A list of all 275 households in 5 bans,

from a census survey in January 1990, was used as a sampling frame and 30% of all households were randomly selected proportionally to the ban's size.

After becoming more familiar with the situation, it was considered that the study should be extended to cover another transmission period in the later year to be explored in more detail. However, at the beginning of the second phase, it was found that some parts of the cohort would be lost due to the local political situation, and the incidence was decreasing. There was a need to increase the sample size, therefore all households in one ban and about 7% more households from the others were included in the second phase. The latter was done by using a proportional random sampling method. The sample size was increased to about 38% of the total population.

3.2.5 Data to be collected :

1. The age and sex of persons,
2. The date of the beginning of the study,
3. The date of the ending of the study,
4. The date of moving out of the residence,
5. The reason for each movement,
6. The distance of the destination,
7. Whether a net was taken along with the mover,
8. The use of other mosquito biting protection methods,
9. The characteristics of the sleeping place,
10. The date of returning to the residence,
11. The date of onset of malaria illness,
12. The type of infection.

3.2.6 Definitions :

A 'movement' - refers to each circular movement, of which a villager left and spent at least a night outside and returned to the residence within the period of observation in each year.

A 'malaria illness' - refers to a parasitologically confirmed malaria episode detected by the routine case detection system existing in the area.

'Incidence of malaria illness' - defined as number of malaria episodes detected, divided by number of person-nights at risk.

'Date of beginning of the study' - refers to the first date that a household member was questioned about any movements. This was the birth date or in-migration date of a new household member.

'Date of ending of the study' - refers to the last date that a household member was questioned about any movements. This was the date of death or out-migration of an existing household member or last follow-up date.

'Onset of malaria illness' - refers to the first date of illness recorded by either the interpreters or malaria workers.

An 'incubation period' - refers to the time elapsing between the initial malaria infection and the first clinical symptom. The incubation periods used in this study for P.falciparum and P.vivax infection are 7 - 15 and 9 - 20 days.

An 'infected period' - refers to a period between the minimum and the maximum incubation periods. These are the periods between day 7 and 15 inclusive for P.falciparum; and day 9 and 20 inclusive for P.vivax.

An 'extraneous infected case' - refers to a case in which the infection most likely occurred during travel outside the residence. A case, which spends at least a night outside the residence during the infected period, is classified as an extraneous infected case.

An 'indigenous case' - refers to the case, which stays inside the residence throughout the infected period.

3.2.7 Data collection methods :

3.2.7.1) Villager movements

The household was visited fortnightly by an interpreter with a special household calender. It consisted of a list of all household members and was designed to enable it to be marked with symbols representing any movements or illnesses. Each household member had a row of a month calender to be marked on. The question was asked whether any household members had spent the night out of the residence during the past 2 weeks. If they did, the date of going out and the date of coming back were asked and marked onto the household calender. At the same time, the other details relating to each movement were asked and recorded in a single page semi-structured questionnaire. A question was also asked about any member who had a headache or fever during the past 2 weeks. The calender was then marked

accordingly and the details of that illness were recorded in a separate structured-questionnaire. A household member who had never stayed in the household during the study period was excluded (see Annex 1.11 for details).

3.2.7.2) Malaria illness

Malaria cases were detected by routine procedures, through both passive and active case detection systems. In the passive case detection system, a patient may go to visit a village health volunteer, village malaria volunteer, health post, or health centre for having a blood slide preparation and a symptomatic treatment including a gametocidal drug (primaquine). The blood slides are collected at least monthly by a malaria worker and brought back to a malaria clinic for examination. The results and curative treatment are taken back to the patient by the malaria worker and the routine historical details on possible sources of infections are recorded but not included in the analysis. Some patients can afford to go to a district hospital or malaria clinic to have a rapid diagnosis and proper curative treatment. At the malaria clinic, after the diagnosis has been made, the patient is routinely interviewed and the possible sources of infection is recorded. At the hospital, blood slides and patient's addresses are kept and collected weekly by the malaria workers. The malaria workers will make a visit to the patient's house and do the routine interview.

In the active case detection system, a malaria worker visits a ban at least every month, collecting blood slides and searching for a fever or malaria suspect case. Blood slides are taken from the suspect case, symptomatic treatment and gametocidal drug are given and the slides are brought back to a malaria clinic for examination. The results are brought back later, curative treatment given and the patient is routinely interviewed on the possible source of the infection. In deep forested areas, a mobile malaria clinic, consisting of a team of malaria workers equipped with a microscope, visits the ban once a month. The blood slides are examined and the curative treatments are given and the patients are interviewed immediately after the diagnosis.

For each malaria patient, the name, address, age, sex, date of onset, date of blood examination, examiner, result of the examination, the drugs given and the possible sources of the infection were routinely recorded and kept at the malaria sector (district level). Copies of all case details were sent to the research team monthly. The name, address, age and sex of these cases were used as references for cross-checking with the references in the previous census data in January 1990. There were many unmatched references due to variation in the quality of recording in the routine case detection system. Any cases with unmatched references were listed and given to the interpreters, who made revisits confirming or rejecting the cases. Malaria workers, who usually work in this area for years and are hence familiar with most patients and their families, were also consulted to confirm the right addresses of those cases. These procedures were carried out carefully to ascertain the reliability of cases detected. All confirmed cases with an onset during 16 July 1990 to 20 February 1991 (this allows for the incubation period) were included in this study.

3.2.7.3) Entomological data :

Several entomological indices were studied in these 5 bans during the same period. These were carried out by another entomological research team and will not be discussed here.

3.2.8 Data processing :

All completed questionnaires were collected and coded once a month by a supervisor. An unclear or a missing form were sorted out and given to the interpreters to complete in the next round of household visits. The completed data were transferred to the Research Institute for Health Sciences in Chiang Mai where the coded data were doubly entered into a computerized form. The entry mistakes were cross-checked and corrected. The data for each movement and illness detected from the mobility register were kept in separate files.

Details of all cases in the study area, confirmed on correct addresses, were entered into a computerized form with the same identification number as appeared in the census registration. Only cases which occurred among the households included in this study were used for analysis. This was sorted out by using a computer software programme.

3.2.9 Data analysis :

Although an analysis at individual level is used, the ultimate unit of analysis is the number of nights each villager spent overnight outside the residence (i.e. a person-night). This is used throughout to describe the pattern of movements. The duration and distance of movement are analysed by the non-parametric method, Kruskal-Wallis analysis of variance. The proportions are analysed using chi-square tests. Two measures of malaria incidence, cumulative incidence and incidence rate, are calculated. The cumulative incidence over the total study period is calculated by using the total number of cases as a numerator and the total persons involved in the study as a denominator. The incidence rate is calculated as the number of episodes per 1,000 person-months at risk. The numerators and denominators are broken down by movement characteristics for calculating the specific incidence. The relative risks are calculated to identify the important risk factors. The relative risks are evaluated using chi-square tests. These are done using the Epi Info computer software program.

3.3 Results

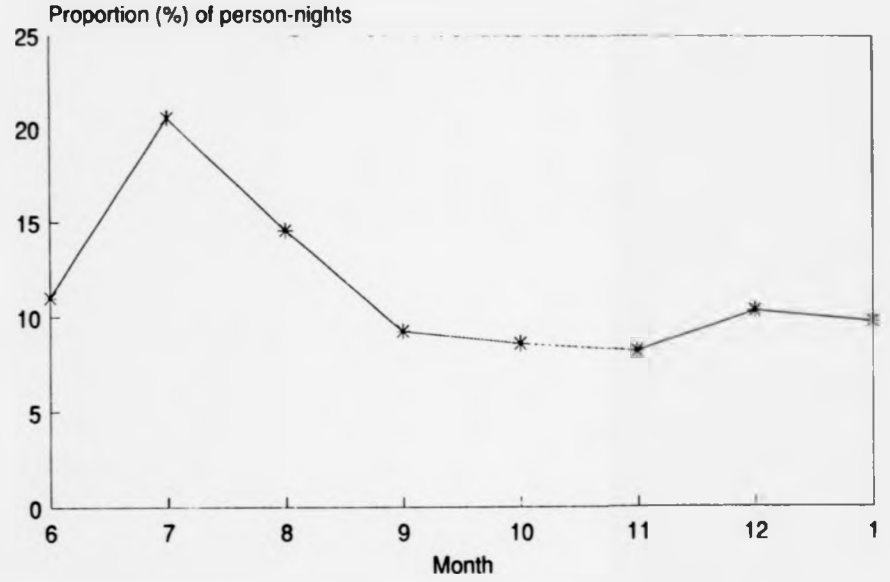
3.3.1 Descriptive results

A total of 494 persons (38.4% of the total population, see Annex 1.1) in 99 households were included over the two periods of study, and 172,929 person-nights altogether recorded on all calenders. There were a total of 1,878 movements involving 364 persons (73.7%). The proportions of movers, by age and sex, are shown in Table 3.1. Adult males predominate ($p<0.001$). The number of movements ranged from 0 to 45 times for each person (median = 2 movements/person). The durations of each movement ranged from 1 to 163 nights (median = 5 nights) (see Annex 1.2). The total movement period was 19,314 person-nights which is equivalent to 11.2 % of the total person-nights recorded. Figure 3.1 shows the seasonality of the proportion of those person-nights. The proportion was highest in July. Figure 3.2 & 3.3 show the trends by age and sex. Analysis of movement duration, by age and sex, reveals that adult males of 15-59 years spend more nights outside their residences than the others (Table 3.2).

Table 3.1 Proportions of movers, by age and sex.

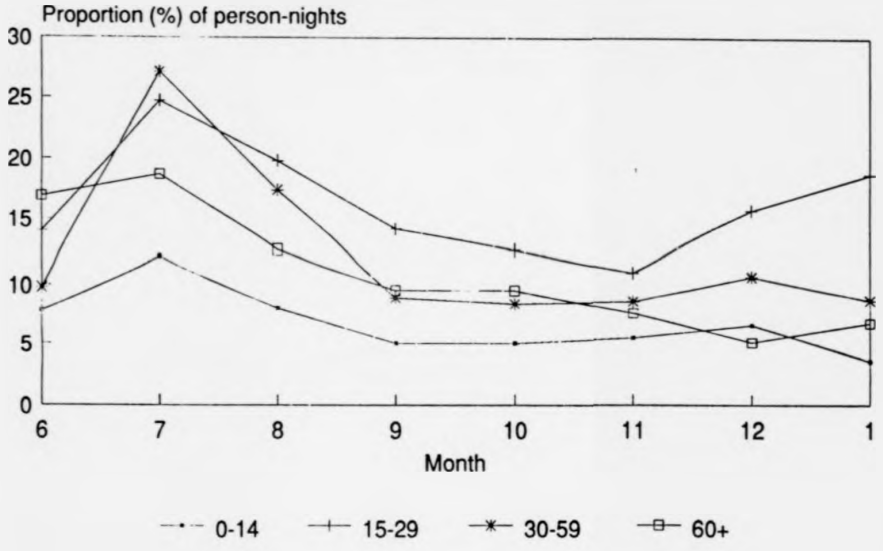
Age (year)	Male			Female		
	Total	Mover	(%)	Total	Mover	(%)
0-14	96	63	(65.6)	84	44	(52.4)
15-29	79	75	(94.9)	68	52	(76.5)
30-59	64	61	(95.3)	65	45	(69.2)
60+	18	14	(77.8)	20	10	(50.0)
Total	257	213	(82.9)	237	151	(63.7)

Figure 3.1 Seasonality of movement outside the residence from June to January.



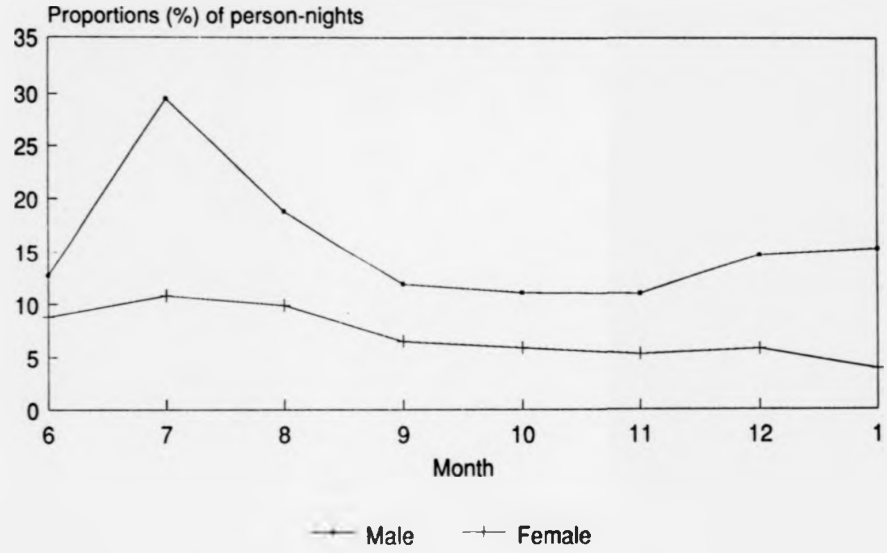
Mae Hong Son, Thailand, 1990-1991.

Figure 3.2 Seasonality of movement outside the residence from June to January, by age group (yr).



Mae Hong Son, Thailand, 1990-1991.

Figure 3.3 Seasonality of movement outside the residence from June to January, by sex.



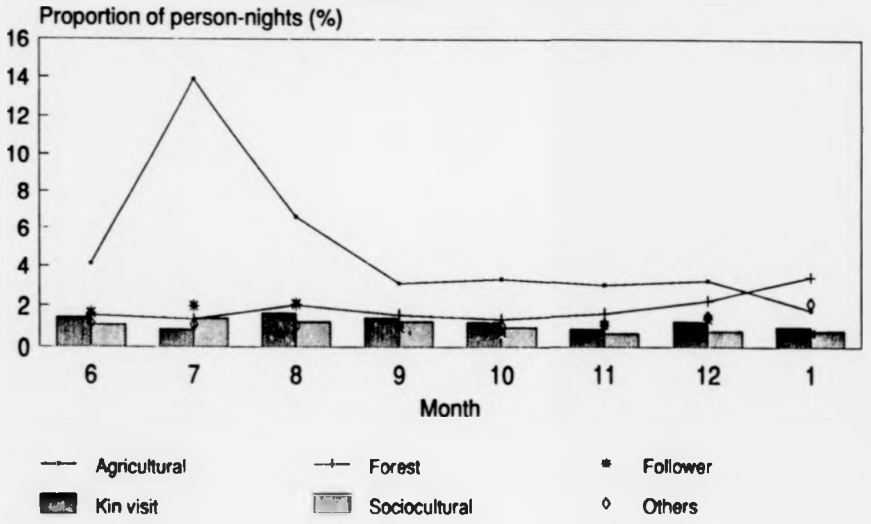
Mae Hong Son, Thailand, 1990 -1991.

Table 3.2 Proportions of movement duration, by age and sex.

Age group (yr.)	Male		Female		Total Prop. (%)
	No. of person-nights		No. of person-nights		
	Total	moved (%)	Total	moved (%)	
0-14	32,721	2,285 (7.0)	26,739	1,468 (5.5)	6.3
15-29	27,046	6,460 (23.9)	25,836	2,096 (8.1)	16.2
30-59	23,085	3,860 (16.7)	23,624	1,798 (7.6)	12.1
60+	6,765	855 (12.6)	7,113	492 (6.9)	9.7
Total	89,617	13,460 (15.0)	83,312	5,854 (7.0)	11.2

There were many reasons for these circular movements (see Annex 1.3), which are grouped and shown in Table 3.3. The first and second most common ones were agriculture (e.g., planting, looking after cattle, harvesting) and forest activities (e.g., logging, reforestation, military service), which amounted to 41.0 and 17.3 % of the total person-nights respectively. Others were passive followers (10.9 %); visiting relatives (10.5 %); socio-cultural activities (education, religious and traditional activities, entertainments, illness and caring for a patient) (8.8 %); and miscellaneous (selling labour in town, other occupations, etc.) (11.4%). Comparing the second to the first phase, the villager spent less time for agricultural and forest activities and more time for the other occupations. Figure 3.4 shows the seasonality of these activities.

Figure 3.4 Seasonality of movement outside the residence from June to January, by activity.



Mae Hong Son, Thailand, 1990-1991.

Table 3.3 Person-nights of movements, by activity.

Groups of activities	Total duration in person-nights (%)
Agriculture (planting, looking after cattle, harvesting)	7,924 (41.0)
Forest (logging, reforestation, military service)	3,341 (17.3)
Followers (children or spouse)	2,111 (10.9)
Visiting relatives	2,025 (10.5)
Sociocultural (Education, religious, entertainments, illness and caring)	1,706 (8.8)
Miscellaneous (Labourer in town, trading, etc)	2,207 (11.4)
Total	19,314 (100.0)

Table 3.4 Types of shelter during movements.

Types of shelter	Total duration in person-nights (%)
Permanent	7,332 (38.0)
Semi-permanent	9,829 (50.9)
Temporary	532 (2.8)
Unknown	1,621 (8.3)
Total	19,314 (100.0)

More than 80% of person-nights outside were spent either in a permanent or semi-permanent shelter, under which a net might be comfortably hung (Table 3.4). However, in only 52.3 % of the total person-nights out was it reported

that a net was taken along, while 35.9 % did not do so and 11.8 % were not known (Table 3.5). The seasonality of the types of shelter and use of nets are shown in Figure 3.5 and 3.6.

Table 3.5 Use of nets when sleeping out.

Was a net brought along ?	Total duration in person-nights (%)
Yes	10,100 (52.3)
No	6,939 (35.9)
Unknown	2,275 (11.8)
Total	19,314 (100.0)

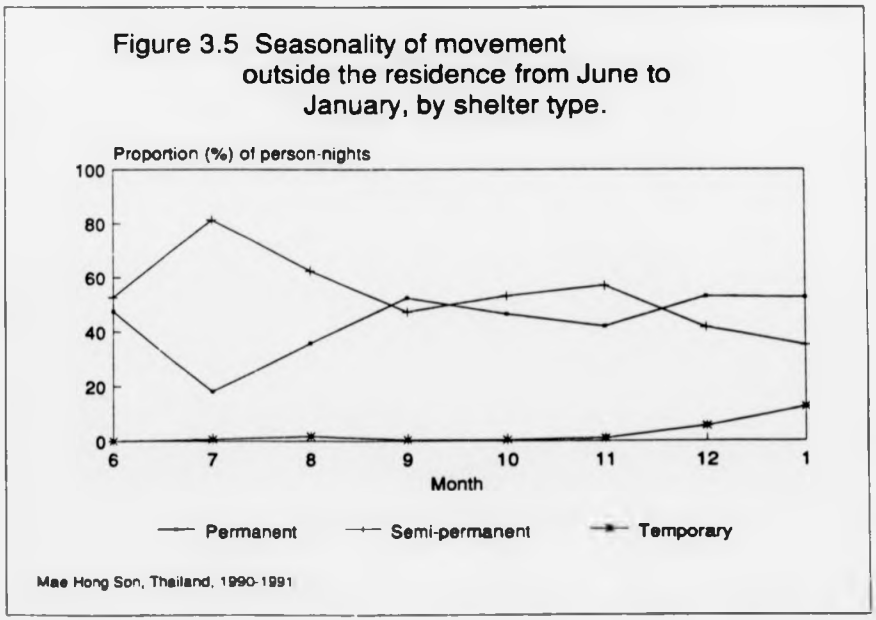
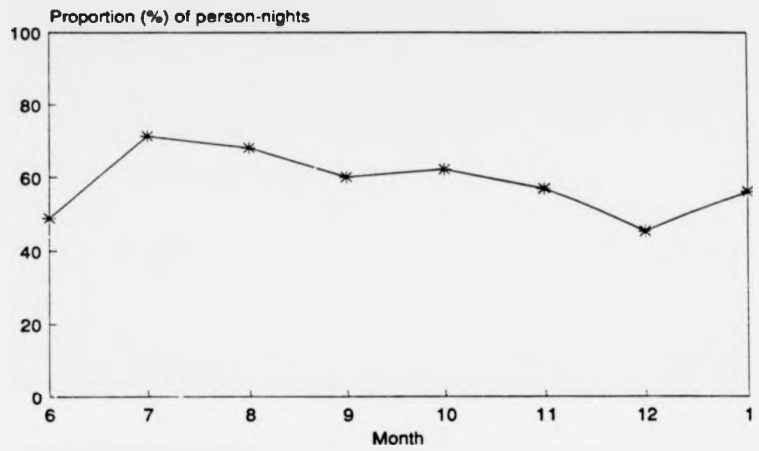


Figure 3.6 Seasonality of movement, with a net taken, from June to January.



Mae Hong Son, Thailand, 1990-1991.

Analysis of activity by age and sex revealed that the movement duration (person-nights) is related to age and sex (Table 3.6 and 3.7) ($p < 0.0001$). Adult males generally dominate all activities and they are almost totally responsible for the forest activity. On the other hand, the passive followers were mainly children of either sex. Forest activity offered the poorest type of shelter and the second was agricultural activity (Table 3.8).

Table 3.6 Activity by age.

Type of activity	Person-nights (%) by age (year)				Total (100%)
	0-14	15-29	30-59	60+	
Agricultural	740 (9)	2,354 (30)	3,816 (48)	1,014 (13)	7,924
Forest	21 (1)	2,476 (74)	775 (23)	69 (2)	3,341
Follower	1,861 (88)	250 (12)	0 (0)	0 (0)	2,111
Kin visiting	81 (4)	1,268 (63)	489 (24)	187 (9)	2,025
Sociocultural	760 (45)	758 (44)	127 (7)	61 (4)	1,706
Others	290 (13)	1,450 (66)	451 (20)	16 (1)	2,207

Table 3.7 Activity by sex.

Type of activity	Person-nights (%) by sex		Total (100%)
	Male	Female	
Agricultural	5,107 (64.4)	2,817 (35.6)	7,924
Forest	3,252 (97.3)	89 (2.7)	3,341
Follower	1,062 (50.3)	1,049 (49.7)	2,111
Kin visiting	1,279 (63.2)	746 (36.8)	2,025
Sociocultural	1,013 (59.4)	693 (40.6)	1,706
Others	1,747 (79.2)	460 (20.8)	2,207

Table 3.8 Activities by type of shelter.

Type of activity	Person-nights (%) by type of shelter			Total 100%
	Permanent	Semi-permanent	Temporary	
Agricultural	623 (7.9)	7148 (90.9)	89 (1.1)	7,860
Forest	814 (24.9)	2015 (61.6)	440 (13.5)	3,269
Follower	616 (52.2)	565 (47.8)	0 (0.0)	1,181
Kin visiting	1989 (98.3)	34 (1.7)	0 (0.0)	2,023
Sociocultural	1520 (99.5)	5 (0.3)	3 (0.2)	1,528
Others	1770 (96.6)	62 (3.4)	0 (0.0)	1,832

(NB - 1,621 person-nights of unknown shelter types are excluded.)

Results of detailed descriptions on the duration, distance and use of nets are shown in Table 3.9. The duration of movement varies significantly among different age groups, activities, types of shelter and net using categories ($p<0.0001$ by Kruskal-Wallis analysis of variance method). The distance of movement also significantly varied among different sexes ($p<0.05$), age groups, activities and types of shelter ($p<0.0001$). The proportions of the total duration with a net taken along varies among all different subgroups mentioned above ($p<0.0001$ by chi-square tests). The villagers tend to bring a net with them when they go to the forest (88.2%), or

sleep in a temporary shelter (87.5%), or spend several nights out (median = 8 nights); and not to do so when they go to visit their relatives or sleep in a permanent shelter or spend only a few nights (median = 3 nights) away. Almost all other mosquito bite protecting methods used during moving were traditional such as a fire or blanket (see Annex 1.4).

Table 3.9 Analysis of the duration and distance of movements, and the use of bednets.

	Duration[1] (median no. of nights)	Distance[1] (median no. of km.)	% of person-[2] nights a net taken along
Sex : Male	5	10 *	62.7 **
Female	5	9	50.7
Age : 0-14	5 **	8 **	43.2 **
15-29	6	10	60.7
30-59	4	9	63.7
60+	5	8	58.8
Activity :			
Agricultural	5 **	6 **	73.2 **
Forest	8	50	88.2
Follower	6	8	51.0
Visit relatives	3	10	7.0
Sociocultural	3	15	44.6
Others	7	30	25.3
Type of shelter :			
Permanent	4 **	11 **	33.2 **
Semipermanent	5	6	74.6
Temporary	10	50	87.5
A net taken ? Yes	8 **	10	
No	3	10	

[1] - Subgroup Analyses using Kuskal-Wallis analysis of variance;
[2] - Subgroup analyses using the chi-square tests;
* - p value < 0.05;
** - p value < 0.0001

3.3.2 Risks of malaria illness

Out of the total 494 persons involved, there were 24 malaria cases (4.9%) involving 28 malaria episodes detected during the total study period (15 months over 2 transmission seasons). Twenty three episodes (82%) were infected by P.falciparum, four (14%) by P.vivax and one (4%) by a mixed infection. When the frequency of movement is grouped by an approximate quartile, the cumulative risks among non-, infrequent and frequent movers are 1.5%, 5.3%, 4.7% and 8.1% respectively (Table 3.10a). This clearly shows the significant direct relationship of a circular movement and malaria illness ($p<0.05$ by the chi-square test for a linear trend).

Table 3.10 Malaria cumulative risks at an individual level, by frequency and duration of movement (data are grouped by an approximate quartile).

a) Frequency of movement

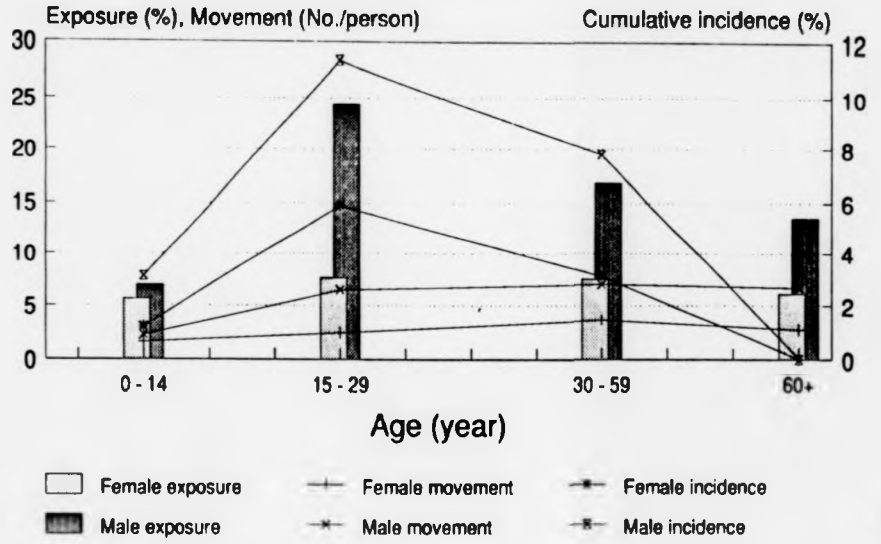
Frequency of movement	Total persons	Number of cases	Cumulative risk (%)	Relative risk
0	130	2	1.5	1.0
1 - 2	133	7	5.3	3.4
3 - 5	107	5	4.7	3.0
6 - 45	124	10	8.1	5.2
Total	494	24	4.9	p = 0.026*

b) Duration of movement

Total movement duration(days)	Total persons	Number of cases	Cumulative risk (%)	Relative risk
0	130	2	1.5	1.0
1 - 20	142	5	3.5	2.3
21 - 60	102	5	4.9	3.2
61 - >400	120	12	10.0	6.5
Total	494	24	4.9	p = 0.002*

* - Significance level by the chi-square test for a linear trend.

Figure 3.7 Cumulative incidence during the 15 month study period, by age, sex, moving frequency and exposure rate.



Mae Hong Son, Thailand, 1990-1991.

A frequent mover, who made more than 5 moves within the 15 month period, carried 5.2 times higher risk than a non-mover according to Table 3.10a. When the total duration of movement is grouped in the same way, the direct relationship of it with the malaria risk is also shown in Table 3.10b ($p<0.01$ by a chi-square test for a linear trend). A long mover, who spent more than the total of 60 nights outside the residence within the 15 month period, carried 6.5 times higher risk than a non-mover. The latter result may be the indirect effects of the number of movements. However, when movers are grouped in the same fashion by the average number of nights in each movement, a long-term mover tended to experience higher malaria risk than a short-term mover ($p<0.05$ by a chi-square test for a linear trend) (Table 3.11). Figure 3.7 shows that the sex-specific cumulative incidence rate, by age group relates more directly with a moving exposure than a moving frequency.

These findings confirm that the risk of getting malaria illness depends on the duration of exposure to various transmission sites outside the residence. Therefore, to continue analysing for the potential risk factors, a person-time approach is used to measure the incidence rate and relative risk. However, analysis of the cumulative incidence by movement activity were also carried out and presented in Annex 1.5.

Table 3.11 Malaria risk of movement, by average duration in each movement (data are grouped by an approximate quartile).

Average number of nights in each movement	Total persons	Number of cases	Cumulative risk (%)	Relative risk
0	130	2	1.5	1.0
1.0 - 4.9	115	7	6.1	4.0
5.0 - 9.9	113	3	2.7	1.7
10.0 - 112.0	136	12	8.8	5.7
Total	494	24	4.9	$p = 0.026^{*}$

* - Significant level by the chi-square test for a linear trend.

Table 3.12 Crude incidence rates, by age, sex and movement.

	Total person-nights visited	No. of epi-sodes	Inc.Rates (episodes /1,000 person-months)	Crude relative risks (95% confidence intervals)
Total	172,929	28	4.86	
a) Age:				
- 0-14	59,460	4	2.02	0.32 * (0.1 - 0.9)
- 15+	113,469	24	6.35	1.00
b) Sex:				
- Male	89,617	20	6.70	2.32 * (1.0 - 5.3)
- Female	83,312	8	2.88	1.00
c) Movement:				
Mover				
-during staying outside	19,314	10	15.53	11.14** (2.4 - 50.9)
-during staying inside	110,565	16	4.34	3.11 (0.7 - 13.6)
Total	129,879	26	6.01	4.31* (1.0 - 18.2)
Non-mover	43,050	2	1.39	1.00

* - p value < 0.05 ** - p value < 0.001

The overall crude incidence rate for the total 15 month period is 4.9 episodes/1,000 person-months (Table 3.12). Children were about 3 times less likely to get malaria illness than adults ($p < 0.05$). Males were at about twice the risk of females ($p<0.05$). There were 10 episodes among the movers with records of movement during the incubation period (see Annex 1.6). These are classified as "extraneous infected episodes" caused by circular movement (see the definitions in 4.6). The incidence rate among movers is 4.3 times higher than that among non-movers ($p < 0.05$). When analysing the risk of each movement, the incidence rate

caused by staying outside the residence during the movement is 11.1 times higher than that of non-movers ($p<0.001$).

Table 3.13 shows the age and sex specific incidence rates when staying in residence and during moving outside. In the former group, the adult male rate is higher than the others. Hence the adult male rate is compared with the rest and it is found that an adult male significantly carries 3.71 (1.44 - 9.57) times higher risk than the others when staying in residence ($p<0.01$). In the latter group, there were no cases amongst the children during moving for age-specific rate calculation because there were too few exposures among the children. The sex-specific rates during moving are similar in both sexes and significantly higher than the rates when staying in residence ($p<0.001$) (see also Annex 1.7). The relative risk of malaria illness from an exposure during moving is 3.8 (1.7 - 9.1) when adjusted for sex. Forest activity significantly carries 6.02 (1.17 - 31.03) times higher malaria risk than the others activities excluding agricultural activity, which carries 1.52 times (0.25 - 9.12) higher risk but this is not significant (Table 3.14).

Table 3.13 Incidence rates of malaria when staying in residence and during moving, by age and sex.

Age group	Male		Female		Total	
	Epis.[1]	Rate[2]	Epis.	Rate	Epis.	Rate
When staying in residence:						
0 - 14	2	1.97	2	2.38	4	2.15
15+	11	7.22	3	1.72	14	4.29
Total	13	5.12	5	1.94	18	3.52
During moving:						
0 - 14	0	0.0	0	0.0	0	0.00
15+	7	18.79	3	20.52	10	19.28
Total	7	15.60	3	15.37	10	15.53

[1] - Malaria episodes

[2] - Incidence rate = Number of episodes/1,000 person-months, calculated based on the person-night data in Table 3.2.

Table 3.14 Incidence rates of malaria during moving, by activity.

Activity during moving	No. of episodes	Incidence rates[1]	Relative risks (95% C.I.)
Forest	5	44.90	6.02 * (1.17 - 31.03)
Agriculture	3	11.36	1.52 (0.25 - 9.12)
Others	2	7.45	1.00

[1] - Incidence rate = Number of episodes/1,000 person-months, calculated based on person-night data in Table 3.3.

* - p value < 0.05

Crude analyses of malaria incidence rates by distance and type of shelter reveal insignificant association between malaria illness and those factors. Further stratified analyses reveal insignificant results due to the small number of episodes and exposures (see Annex 1.8 and 1.9).

3.3.3 Possible protective effects of a net

Table 3.15 shows the incidence rate of malaria during moving, analysed by whether a net is taken along or not, and whether the net is from a household which brought their nets for impregnation in February. There are 1,330 person-nights of moving by the treated net group in which one episode occurred, and 8,770 person-nights with 6 episodes by the untreated net group. The incidence rates among the mover with a treated net, an untreated net and without an untreated net taken were 22.6, 17.1 and 13.0 episodes/1,000 person-months respectively. The crude analysis shows that having taken a treated or an untreated net along carries a slightly higher risk than not doing so, but this is not significant. However, this is strongly confounded by the type of activity. For further stratified analysis by activity, the treated net group was excluded because it has only one case and there may be a self-selected bias of bringing a net to be impregnated among people who tend to realise the risk of malaria. The data related to agricultural and other activities are pooled and compared with forest activities (Table 3.16). The relative risk among forest movers is not calculable

because there is no episode occurring among movers not taking a net with them. This may be because in the forest group, there are only 390 (12%) person-nights contributed by forest movers who enter the forest without taking a net with them. The overwhelming majority of forest movers (88%) bring nets with them entering the forest. The relative risk of taking a net in the other activities is 0.73 (0.12 - 4.38). This is equivalent to 27% protective effects. However, the number of episodes is too small to get a significant result.

Table 3.15 The incidence rates according to whether a net was taken.

Net taken	Person-nights	Epi-sodes	Inc.[1] rates	RR [2] (95 % C.I.)
Yes :				
-net treated	1,330	1	22.6	1.74 (0.18-16.71)
-net un-treated	8,770	6	20.5	1.58 (0.40-6.33)
No	6,939	3	13.0	1.00
Unknown	2,275	-	-	-
Total	19,314	10	15.5	

[1] - Incidence rates = number of episodes/1,000 person-months.
[2] - Crude relative risks with 95 % confidence intervals.

Table 3.16 Relative risk of malaria, by activity and whether a net was taken.

Activity	Net taken	Person-nights	No. of epi-sodes	Inc.[1] rates	RR [2] (95 % C.I.)
Forest					
	Yes	2,814	4	42.6	not
	No	390	0	0.0	calculable
Others					
	Yes	5,956	2	10.1	0.73 (0.12-4.38)
	No	6,547	3	13.7	1.00

[1] - Incidence rates = number of episodes/1,000 person-months.
[2] - Crude relative risks with 95 % confidence intervals.

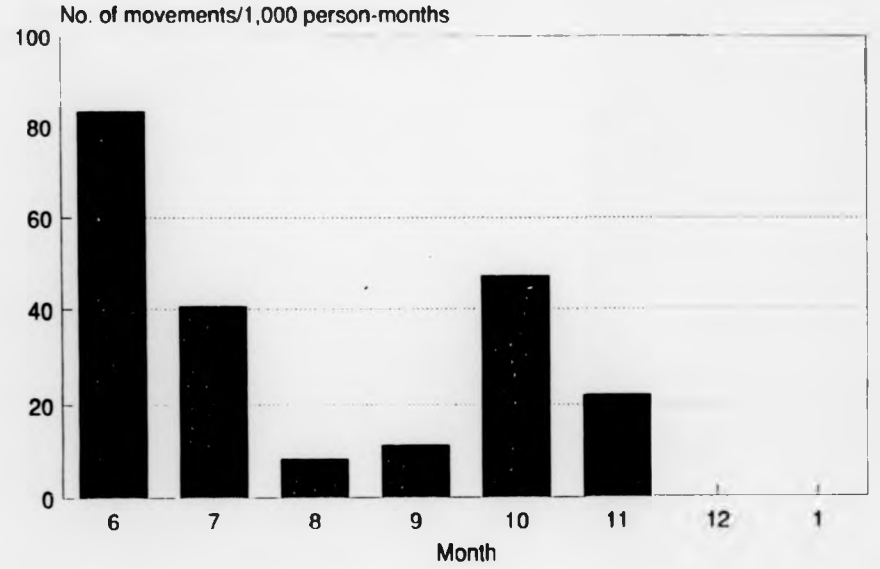
3.3.4 Late night movements

The possibility of getting malaria from late night or early morning exposures was raised after the first phase of the study. In the second phase, a late night activity was also recorded aimed at exploring this possibility. During June 1991 to January 1992, there were 69 such occasions. All were for the forest activity within 3 kilometres (mean 1.41 km.) from the residence. None of them fell into the incubation periods of the cases in the second phase. Only 2 (2.9 %) were females. One third of the total were children (Table 3.17). Figure 3.8 shows the seasonality. The first and second peaks are in June and October respectively.

Table 3.17 Late night forest activity, by age and sex.

	Sex		Total
Age	Male	Female	
0 - 14	23	0	23 (33.3%)
15 - 29	30	2	32 (46.4%)
30 - 59	14	0	14 (20.3%)
Total	67 (97.1 %)	2 (2.9 %)	69 (100 %)

Figure 3.8 Seasonality of the late night activity from June 1991 to January 1992.



Mae Hong Son, Thailand.

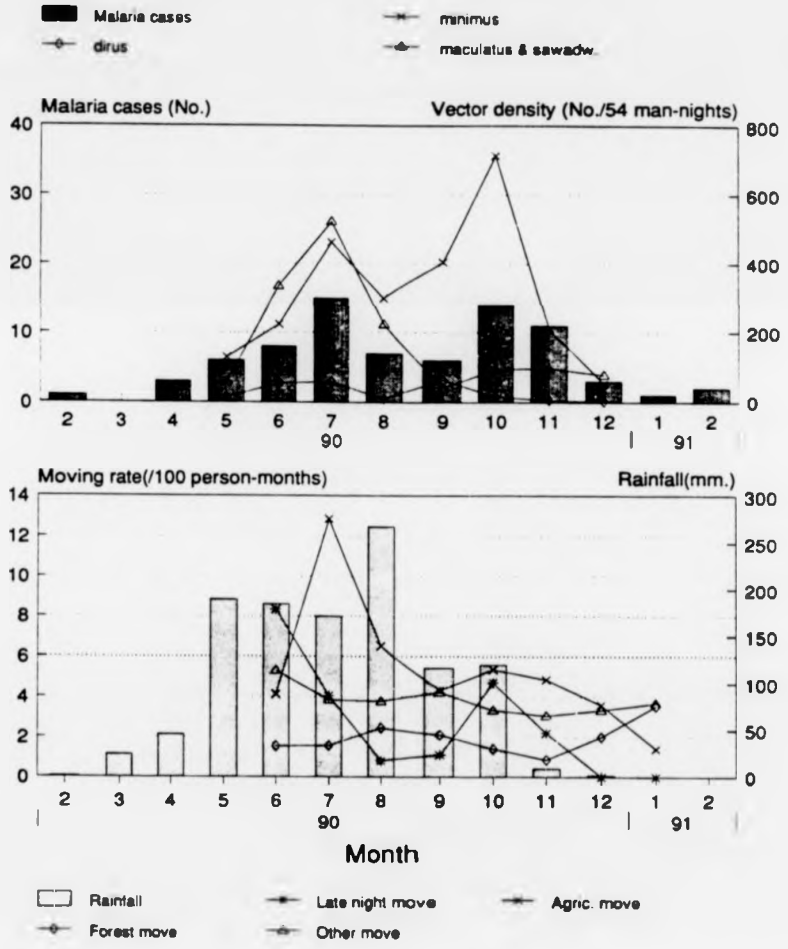
3.3.5 Seasonality of movements, malaria incidence and human-vector contacts

The seasonality of movements is analysed together with the seasonality of 4 potential vectors found in the area, An.minimus, An.dirus, An.maculatus and An.sawadwongporni, amount of rainfall and number of new cases in the study area (Figure 3.9). The mosquitoes were collected by Mr. Pradya Somboon, another PhD student working on the entomological indices in the same area. This part of the analysis is shared with him. An aim of this analysis is to understand the overall relationship between the rainfall, the vector dynamics, the population movements and the malaria seasonality.

The vector density is the number of vector mosquitoes caught by human bait both in the residential area and farm huts from May 1990 to December 1990. The number of vectors caught in the residential area is very small and is pooled with those from the farm hut catch. This would reflect the forest fringe rather than the forest situation. Densities of An.maculatus and An.sawadwongporni are pooled due to their ecological similarity. Movement data was not collected before July 1990 and during February to May 1991 so the rate in June 1990 is estimated from that in June 1991. All the late night movements are also estimated from 1991 data. These are used as the best estimate because no such data in 1990 are available.

There are two peaks of malaria illness. The first is in July and the second in October. There were no cases in March. This pattern corresponds with patterns of vector density, agricultural and late night movements. An.minimus is the most prevalent vector. It has 2 peaks in July and October but the former peak is smaller than the latter peak. An.maculatus and An.sawadwongporni are predominant during June to July and decreased to a low level throughout the rainy season. An.dirus is very rare in this forest fringe setting. Late night movements is the highest in June and decreasing when the agricultural activity increases to its first peak in July. Both of them increase to a smaller peak again in October. Forest activity is very low during the rainy season but starts to increase in December when there is no rain. The rising trend is apparently continued into the dry season when the observation ends in January. The other activities show a slightly decreasing trend since the observation started in June and a slightly increasing trend in January.

Figure 3.9 Seasonality of malaria cases, vectors, rainfalls and movements.



3.4 Discussion

3.4.1 Design of the study

Taking history of a movement from a malaria patient is the easiest way to learn about movements among cases. This is a routine procedure performed by malaria workers to classify a case as indigenous or imported (Malaria Division, 1991), and the results are helpful in guiding the control activities. However, these also contain errors and limitations. The history taking is always done after a diagnosis has been made. This introduces information biases into the record. The malaria patient may not be able to recall the detailed date and activities, especially when the diagnosis is made, through a primary health care system, several weeks later than an onset of the illness. With such uncertainty, common movements tend to be blamed and are recorded by a malaria worker who believes that there is minimal or no transmission occurring in the community. In addition, the direct contribution of exposures among cases to the incidence, without knowing the proportion of exposures among healthy people, can be misleading.

A cross-sectional study can properly measure the relative risk of movement and other risk factors. However, these methods can capture only a small portion of the population movements (Radloff, 1983). A serial cross-sectional study with more than one fixed-time point can yield more details with an increasing number of fixed points. However, the yields are limited to only a net movement between the fixed points and movements with a duration shorter than the interval are missed (Radloff, 1983). Therefore, a classification of population into a presentee, an absentee and a migrant may not represent the true nature of movement. The misclassification can lead to an underestimation of the relationship between a movement and its consequences. This may partly explain the apparently small differences in malaria prevalence among different movement categories in the Garki Project, from which it was concluded that there was no difference in respect to malaria, either between those who were leaving and those who were already there, and that on the absence of control measures the local epidemiological situation is not significantly affected by the mobility of part of the population studied (Molineaux and Gramiccia, 1980). Life time movements can be found retrospectively by a life history matrix (Balan et al. 1969; Radloff, 1983). This may be adapted to measure recent short-term movements

but can suffer from recall difficulties and the results may not be reliably related to a malaria illness. Therefore, to achieve comprehensive results to understand the situation in this area, a prospective study has to be used.

A concurrent case-control study (Butrapom et al, 1986; Fungladda et al, 1987) can properly detect the malaria risks of movement with lower costs compared to a cohort study, but can still suffer from recall biases and loss of precision on movement estimates. A cohort approach can yield very rich details on movement (Singhanetra-Renard, 1981) as well as the absolute malaria incidence rate related to it. The difficulties will depend on the area covered by the study. It is extremely difficult and expensive when trying to do a quantitative study on detailed spatial and temporal movement on a macro scale. Therefore, it would be appropriate to initiate a quantitative study of movement and its consequences on a micro scale.

Measures used to describe movement can be the proportion of people who move at least once, or an average number of movements per person (Long, 1970), during a fixed period. These are not adequate for analytical purposes especially when the consequences of movement are time related. Standing (1984) suggested the proper measure should include the duration of movement. Peppiatt and Byass (1990) used the person year approach to study the risk factors for malaria among British missionaries living in tropical countries. For studying the local malaria transmission, the unit used in the analytical studies should represent the smallest unit of exposures.

A person-night unit was considered to be adequate at the beginning. At the middle of the study, a unit smaller than this was considered because a movement for several hours during the night time had been misclassified as a non-movement. The study was expanded to include this night movement in the second year. However, the results show that this type of movement is not attributable to the malaria incidence in this area (see 5.4). Hence, the person-night is used for detailed analysis.

3.4.2 Tools

3.4.2.1 Detection of movements:-

The sensitivity and specificity of measuring movements partly depend on the definition of movement, which depends on the objective of the measurement (Radloff, 1983). In general, both spatial and temporal boundaries are needed to define a clear definition for a study of movement. In this study the short

term movement leading to an exposure to malaria transmission foci outside the residence has been a subject of interest. Therefore, the residential area is used to define the spatial boundary of movement. The overnight absence from the residential area is used because this is directly related to the biting time of malaria vectors. The longitudinal repeated household survey is very sensitive in detecting time and duration of short term movement, especially when a movement calender is added. However, the reliability of movement details can also be subject to a recall difficulty. This depends on the interval of movement recording. The ideal would be a daily self-administration by household members. This needs a considerable level of enthusiasm and literacy in the household. Only a few Karen households produced a reliable self-administrative mobility registration so repeated interviewing was needed. One week visiting interval is suggested for reliably recalling a morbid event (Smith and Morrow, 1991). Resources available in this study allowed for a fortnightly interval, which should be reasonable for recalling a rather obvious timing and duration of movement. However, this may not be short enough for effectively detecting several hour movements at night.

The additional semi-structured questionnaires, used for recording details of movement, are also subjected to recall bias. Recall problems increased among the frequent movers who were seldom available at the time of interview. Other available sources of information in the household at the time of interviews were therefore used.

3.4.2.2) Detection of cases:-

Only 5 (18%) out of 28 episodes were detected by the active case detection system, which may be more sensitive in detecting malaria cases than the passive system. The sensitivity of the overall case detection systems may be low. This may be a cause of having a rather small number of cases in this study, which can lead to an underestimation of the incidence rates and relative risks. However, results from mass blood surveys (see next chapter) produce quite a small number of positive cases. Only 2 (7%) of additional cases were found. This suggests that the sensitivity level of the existing case detection systems may be enough, so the cases found by mass blood surveys are excluded from analysis due to a failure to meet the definition of malaria illness. The reliability of the system depended on the quality of the diagnosis, which should be high because parasitological criteria were used to

diagnose the cases.

3.4.3 Definitions

3.4.3.1) Malaria illness

The definition for an illness is subjective and socially dependent to some extent. People perceive and behave differently in different cultures. All villagers in this study are of the Karen ethnic minority. Their perception of malaria illness should be quite homogeneous. The high proportion of cases detected from the passive detection system is reassuring that most malaria cases in this study were aware of their illness and sought help from the health care system. The definition based on the routine case detection system in this study should be adequately representative of what the community perceives as its burden.

3.4.3.2) Incubation period

In malariology, the incubation period is related to the prepatent period. The prepatent period is the minimal time elapsing between the initial sporozoite injection and the first appearance of parasites in the erythrocytes (Garnham, 1980). The incubation period is the time elapsing between the initial malaria infection in man and the first clinical manifestation (WHO, 1963). The latter will be always longer than the previous by at least 2 days (Garnham, 1980). The incubation period is dependent on the type of infection, the strain of parasite, the number of sporozoites injected and the immune status of the host. The shortest incubation period of P.falciparum and P.vivax are 7 and 9 days (Coatney et al, 1950; 1971; Garnham, 1980). The longest period for P.falciparum is 27 days (Coatney et al, 1971). In general, it is about 14 - 15 days (Bruce-Chwatt, 1980; Harinasuta and Bunnag, 1988). For P.vivax, it is extremely varied and can be more than 300 days (Garnham, 1980; Harinasuta and Bunnag, 1988; Li et al, 1989). The P.vivax strain in this area is likely to be similar to type I, Chesson strain (Harinasuta and Bunnag, 1988). Therefore, in this study, the usual incubation periods for P.falciparum and P.vivax are assumed to be 7 - 15 and 9 - 20 days.

3.4.3.3) Extraneous infections

In this area, the case which gets an infection and moves into the community is generally called an imported case (Malaria Division, 1991). This may be confused with an infected immigrant. Ross (1911) clearly defined terms which are

well suited to the spatial and temporal dimension of movement. He classified an infected immigrant as an imported case and an infection contracted outside the residence due to the circular movement as an extraneous infection. Though the latter term is not generally observed in the literature , compared to the previous one, it is well suited to the epidemiological situation in the study area.

3.4.4 Results

3.4.4.1) Descriptive results

a) The representativeness of samples

Males in the age group 15 - 29 years and old females are slightly more represented than the rest (see Annex 1.1), but these are not statistically significant. The results of this study should sufficiently reflect what is going on in this locality.

b) Size of movements

About 74% of the samples had at least one movement over the 15 month study period with a median of 2 movements per person. More than 80% of the total 1,878 movements have a duration shorter than 2 weeks and the median is 5 nights (see Annex 1.2). Singhanetra-Renard (1981) reported the size of villager mobility in a district in Chiang Mai province. She found that more than 90% of all movements had a duration of less than one day and if this daily movement was excluded, more than 80% of the rest had a duration of less than 1 week. Similar findings in Indonesia were also reported by Mantra (1981). These findings suggest that short term movement is common. When the proportion and duration mentioned above are put together, the proportion of the total person-nights involved in all movements is 11.2%. It can be directly inferred that during a transmission season from June to January, a villager in this area spends about 11 nights in every 100 night period, or roughly one tenth of his time, outside the residence. This estimate is directly interpretable in terms of the size of exposure to malaria transmission foci outside the residence. However, in some circumstances the movement process is more important than the duration and the number of movements may be more useful. A long distance movement from a low endemic area across a high transmission zone to another low endemic area is an example. In this case, the duration from moving out of the residence to returning back would be classified as the movement duration under the definition of movement in this study and the resulting person-night estimate would

overestimate the extent of the exposure.

The predominance of adult males involved in movements is a common finding in developing countries (Singhanetra-Renard, 1981; Mantra, 1981). Agricultural works are the major occupation in this area contributing to the majority of movements (41%). Forest activities are the second income generating occupation in this area. These are common findings of villager movements in the forested area described by many observers (Singhanetra-Renard, 1986; Butrapom et al. 1986; Fungladda et al. 1987; Kondrashin et al. 1991). Apart from traditional rural forest activities, the special movement adding to this category in this area is the forest patrolling activity. A few young adult males in the village were recruited for governmental and military service to suppress illegal activities which occurred in this forest-border setting. Analysis by age (Table 3.6) and sex (Table 3.7) showsthat forest activity is almost exclusively by adult males who also considerably share most of the other activities. Although children have spent most of their time in residence, they can be subjected to malaria infection when they move with their parents.

c) Type of shelter and the use of nets

Most of the time movers slept in the permanent and semi-permanent type of shelter. This data is less reliable than the activity data considering 8.3% slept in an unknown place (Table 3.4). The proportion which slept in permanent and semi-permanent types, however, outweighed the uncertainty. This reflects that a bed net can be used quite comfortably during moving, as long as it is taken along. Table 3.5 shows the majority of villagers took a bed net with them during moving but the level of uncertainty is also of considerable size (11.8%). The majority of this uncertainty is in the children group moving with their parents (see Annex 1.10). If the unknown group is excluded, the estimated proportion which took a net with them will be 59.3%. This estimate is lower than that of 69.7% reported by Chitprarop et al (1986) studied in another area with rural Thai villagers.

Results from the other survey in this area (see next chapter) revealed that in about 12 % of farm huts, there were bed nets permanently kept there and villagers need not take any nets to the farm. These were classified as having taken no nets with them. This is partly responsible for the underestimate. Another reason is a very low rate of taking nets during visiting relatives (7% in Table 3.9). This is

easy to understand because the relatives would have prepared nets for this purpose. This can also be the reason for the low rate of nets taken when movers slept in permanent shelters. Results from the other household surveys showed that about 16% of the surveyed household kept some of their nets for such circumstance. If these estimates from the household survey are used to correct the proportion protected by nets in agricultural activity and visiting relatives (Annex 1.10 and Table 3.5), the corrected estimate is about 66.8%, which is close to that reported by Chitprarop et al (1986). The high rate of net taking in forest and agricultural activities indicates that villagers in this area are very familiar with using bed nets and they know quite well in which circumstances they should take nets with them, given that they have enough nets to do so.

3.4.4.2) Risk factor analyses

When analysing the cumulative incidence using an individual as a unit of analysis, it is clear that the frequency and duration of movements has a direct relationship with the risk of malaria illness (Table 3.10, 3.11 and Figure 3.7). However, when trying to relate the activity and other movement characteristics with malaria illness, many limitations are found. A frequent mover has different types of activity as well as shelter and way of using nets. The risk factors of interests are mixed up in a unit of analysis. To measure an exclusive effect of each type of activity on the cumulative incidence in this way, the frequent mover involved in more than one type of activity is separated out. Analysis of the remaining data shows that a forest mover carries the highest risk, about 16 times more than a non-mover ($p<0.01$, see Annex 1.5). This is diluted by a half when the forest mover is also involved in other activities. These risks are not directly related to the size of exposure and the incubation period of malaria illness is not taken into account. For example, 2 malaria episodes occurring 2 and 12 months after returning from only 2 days of agricultural works are counted as only one case and the agricultural activity is wrongly blamed for these episodes (episode no. 16 and 23 in Annex 1.6). To put an incubation period definition on the cases, more cases are needed because the data on mixed exposures will have to be discarded under this scheme of analysis.

A person-night unit does not contain a mixture of exposures as does an individual unit. The analyses are allowed to include all available data and relate the

malaria incidence rate directly to the size of exposures of various risk factors. All episodes are included in the calculation of incidence rate. This is because a malaria episode does not protect a patient from a reinfection and a later exposure to any risk factors can cause another episode after the specific incubation period. During the weeks after a radical treatment of malaria, the patient might have had a sufficient blood level of the schizontocidal drug to be protected from a reinfection. However, the incidence rate in this area is low. The subtraction of the patient's person-nights for a few week after the radical treatment results in a negligible increase in the incidence rate. Hence, it is more convenient to include them in the denominator of the incidence rate. The chance of having none or one malaria episode from a person-night exposure, after a proper incubation period, will be assumed to follow the Poisson distribution.

This approach is not free from limitations. The possible interval of incubation period can cause uncertainty as to which unit of exposure has contributed to the episode. The larger the interval the more uncertain it is. For example, episodes no.11, 14 and 17 (see Annex 1.6) clearly demonstrate this uncertainty. They may be attributable either to movement or staying in residence. It can also happen that the uncertain episodes may be attributable to more than one type of movement. This can happen to both short and long term movements although it is likely to be more in movement with a duration less than the incubation interval (7 - 15 and 9 - 20 days for P.falciparum and P.vivax respectively, in this study). However, these uncertain occasions can be rare if there is no transmission in the residential area so that all episodes can be attributable to movements (Peppiatt and Byass, 1990; as an example).

In this study, to avoid this uncertainty, the incidence rate amongst non-movers, 1.39 episodes/1,000 person-months (Table 3.12.c), should be regarded as the best estimate of the risk of malaria when staying in residence. If those 3 uncertain episodes are excluded, the incidence rate during moving will be reduced from 15.53 to 10.87 episodes/1,000 person-months. This corrected rate is still significantly 7.8 times (1.62 - 37.55) higher than the rate when staying in residence ($p<0.01$). Therefore, the true incidence rate attributable to movement is somewhere between 10.87 to 15.53 episodes/1,000 person-months and the relative risk between 7.8 to 11.14 times. The corrected rates attributable to forest, agricultural and other activities

are 35.91, 7.57 and 3.73 episodes/1,000 person-months (Table 3.14). These result in the same trend as when there is no correction but the detection of risk factors contains less false positives and more false negatives. The large difference of vector density between village and farm hut catch can easily explain these findings. The farm huts are located in forest fringe settlements. The vector density in the forest can be even higher than in the farm huts. The duration of forest movements is also longer than the others. Therefore, the forest movers are more exposed to the high vectorial capacity and subjected to a greater chance of getting malaria infections. However, when comparing the proportion of malaria illness attributable to various activities, the majority of illness occurred amongst movers when they stayed in residence. This contradicts the finding of very low vector density in the village.

3.4.4.3) Sex specific rates and late night movements

It is interesting to see the similarity of the incidence rates between different sexes during moving and amongst children and females when staying in residence. The apparently high malaria morbidity in males may be explained by their high rate of exposure outside the residential area. The predominance of the adult male incidence rate when staying in residence may be a result of two possible causes.

The first is an exposure nearby the village, during the dusk and dawn. This type of exposure is missed from the study due to the difficulties in recording it. Although efforts were made to detect late night movement, the fortnight interval of the household visits were too long for effective recall of this type of movement. Only special occasions of this type might have been detected (Table 3.17) and many of them missed. However, this again, shows the predominance of adult males. Although none of the late night movements contributed to malaria episodes the sex specific pattern is directly correlated with the sex-specific rate during staying in residence. This suggests that the majority of episodes may be attributable to this type of movement.

The second may be an exposure in the forest during performing an illegal forest activity. This type of movement involved only adult males and was likely underreported. Therefore, the cases were misclassified and this led to the conflicting high incidence rate amongst adult males when staying in residence.

3.4.4.4) Possible protective effects of a bed net

The net using behaviour during moving is extremely difficult to observe. A direct question can lead to overestimation due to the willingness of the villager to please interviewers of this study. A net taking behaviour was used as a proxy indicator to avoid this bias. However, it results in an underestimation. This can dilute the chance of detecting possible protective effects of a bed net. The small number of malaria episodes and the huge uneven distribution of person-nights make it difficult for stratified analysis especially in the forest activity. The analysis of net taking behaviour in other activities shows a 27% protective effects but this is not statistically significant. However, this is an underestimation due to the misclassification bias of this behaviour mentioned previously. The actual size of the effect may be larger than this. Other studies using a case-control approach (Butraporn et al. 1986; Fungladda et al. 1987) reported higher protective effects. This confirms that the malaria transmission in this area can be partly prevented using just untreated bed nets for individual protection.

3.4.4.5) Possible protective effects of treated bednets

The number of episodes was too small for stratified analysis to explore any possible effects of a treated bed net. However, Kamol-Ratanakul and Prasittisuk (1992) used a randomised control trial to study the effectiveness of permethrin-impregnated bed nets against malaria amongst migrant workers in eastern Thailand and reported about 41% individual protective effects compared with untreated bed nets. They also suggested the integration of this method with large-scale primary health care programmes. The community-wide impregnation programmes comparing pyrethroid-treated with untreated bed nets were also conducted in this area (see next chapter).

3.4.4.6) Man-vector contacts during movement

The pattern of rainfall seems to determine the vector ecology, population movement and malaria transmission. After the rains had started in March, the density of all potential vectors increases and when they decrease so do the vectors. An.maculatus and An.sawadwongporni have similar dynamics so are pooled together and constitute a major single peak during the mid rainy season. An.minimus has 2 peaks, a small one during the mid season and large one during the late season

(Figure 3.9). This is because it prefers slow running streams. The heavy flooding at the middle of the rainy season reduces its population before increasing again after the flooding dries out. These may suggest that An.maculatus and An.sawadwongporni play a more important role in malaria transmission during the early and mid rainy season, and An.minimus is the major vector responsible for the later peak of transmission. The main agricultural movements occur during the early peak when An.maculatus and An.sawadwongporni are predominant, whereas there are less movements during the second peak when An.minimus predominates, suggesting that movements at this time with this vector are more likely to result in infection. An.dirus density is so low that it may be negligible in the forest fringe setting.

Before the major planting season, villagers frequently spent time out during the night. Most late night activities are hunting and fishing. Some might have just returned from visiting relatives and other activities, to be ready for the planting season in July. Almost all agricultural activities in June to August are planting, which needs to be finished in a short time to allow the crop to get enough rain for good yields. All work forces in the family are needed in this process. This causes a sharp rise in the proportion of moving exposure due to many villages involved in the process in a very short time. The proportion drops rapidly after they finish their planting works and return to the residence. After this, some of them have more time to do the other activities including forest activities. When the rice is ripe and ready for being harvested, it is interesting to observe that the harvesting work does not need as many man-days per month as the planting period and tends to be spread over a longer period of time. This corresponds with the sustained peak of malaria cases in November. Without the necessity to finish harvesting as quickly as planting, villagers worked in the farm not far from their residence and did not need to stay overnight at the farm hut. They chose to go to the farm very early in the morning and walk back home late in the evening. Hence, they exposed themselves to An.minimus which has become an early and late night biter under long term pressure of DDT spraying. This type of exposure was missed from the fortnight household visit and many cases who got infections in this way might have been wrongly attributed to an exposure within the residential area and cannot be totally explained by the very low vector density.

3.4.4.7 Further studies

The limited research resources allowed this study to explore only the relationship of circular movement and malaria illness during the transmission season. Results of this study suggest the usefulness of the methodology for quantifying the complicated relationship of movement and malaria transmission dynamics, especially in the area equipped with a good case detection system. This prospective method allows for the more rigid criteria of incubation period than that used in many case control studies (Banguero, 1984; Butraporn et al. 1986; Fungladda et al. 1987). This also clearly shows the detailed difficulties in attributing an illness of relatively long incubation period to mixtures of short term exposures.

More studies are needed to confirm the importance of several hour movements nearby the village. These can form the bases for epidemiological evaluation of the possible impacts of repellents and their cost-effectiveness. This protective method seems to be the only tool to protect villagers under these occupational patterns of movement. The repeated household interviews weekly or less throughout the whole year will yield more details of several hour movements. These studies should cover the whole year to see also the possible role of movement in maintaining the infective reservoirs in the forest during the dry season.

3.5 Conclusions

3.5.1 Short term movements during the transmission season were common. About 74% of villagers moved at least once. On average, villagers spent about 11% of their nights outside the residence during the season. The first and second common reasons were for agricultural (farming, harvesting and looking after cattle) and forest activities (logging, reforestation works and forest patrolling) respectively. A small number of several hour movements for hunting and fishing during the night were also detected. This is expected to be largely underestimated. Adult males predominated in all types of movements.

3.5.2 In general, about 60% of movers took a bed net with them. They tended to do so when they entered the forest (88%) or went to the farm (73%), slept under the temporary (87%) or semi-permanent shelters (75%), or when the moving duration was long (median = 8 nights). Very few of them took a bed net when they went to visit their relatives.

3.5.3 The malaria incidence was directly related to the number and duration of movement. The risk of malaria amongst movers during moving can be at least 7.8 times higher than the non-movers staying in residence. The incidence rates during moving in both sexes were similar. Forest activity carried the highest risk, followed by agricultural and other activities respectively.

3.5.4 An attempt at measuring the possible protective effects of untreated bed nets during moving revealed about 27% effectiveness excluding forest activity, with a wide range of statistical error, due to the small number of episodes.

3.5.5 Analysis of the seasonality of malaria illness in relation to rainfall, vector density and movement together with the high incidence rates amongst adult males during staying in residence, suggests the importance of agricultural activity and several hour exposure during the dusk and dawn.

3.5.6 More extensive studies covering the whole year may elaborate more details about the possible role of movement in maintaining the infective reservoir in the forest.

Chapter 4

The effectiveness of lambda-cyhalothrin bednet impregnation programme.

4.1 Background information

Since the advent of DDT in the late 1940's, indoor residual insecticide spraying became the most important single measure for global malaria eradication programmes. As a result, many residual insecticides were developed simultaneously and evaluated for this purpose. The eradication programme has, unfortunately, failed in many countries and been replaced by a broader malaria control scheme using a primary health care approach. Many old and forgotten control measures have been evaluated again, one of which is the mosquito net. The use of mosquito nets can be traced right back to the sixth century B.C. (Lindsay & Gibson, 1988). It was widely used in many parts of the world to protect against insect bites. Later it has been recommended for personal protection against malaria. Nevertheless, people use it mainly for preventing insect nuisance. Although its potential for reducing man-vector contact of night-biting anophelines may be considered, its impact on the diseases conveyed by the vectors is rarely appreciated. Surprisingly, there have been few studies of its efficacy on diseases, considering its old age and worldwide distribution. Recently, there have been an increasing number of studies on the protective efficacy of bed nets especially when treated with a residual insecticide. The results so far are very encouraging. This report is an attempt to review all relevant aspects relating to the effectiveness of bednets, especially impregnated ones, used in controlling malaria, the most important vector-borne disease in the world.

4.1.1 Untreated bednets in malaria control

Lindsay and Gibson (1988) traced a history of mosquito nets back to the sixth century B.C.in Egypt. They later seemed to be developed independently in many isolated communities around the world. The original idea was probably for uninterrupted sleep. Most of the early records of use of bed nets were among the aristocrats and they were luxuriously decorated. Later, the idea spread and they were

used by women, children and fishermen. Nowadays, mosquito nets are still commonly used among ordinary people in the tropics.

4.1.1.1) Proper use of untreated nets

In order to derive maximum protection, Covell, in 1943 (quoted in Farid 1988), suggested as follow:

1. The net material should be white to allow easy detection of mosquitoes; all sides should consist of netting (with only a lower strip of calico) to allow free access of air.

2. A large bed and net should be used, in order to minimise the possibility of pushing bare hands, knees or elbows against the net during sleep, so allowing mosquitoes to bite through the net from the outside.

3. The net should be tucked in all round, under the mattress.

4. If the net was lifted from the bed by day, the bottom should be closed and it should be let down before dusk, stretched and evenly tucked under the mattress.

5. Upon retiring the net could be loosened along one side of the mattress just sufficient to allow the person to crawl into bed, and then be tucked back in place again from the inside.

6. Any rents or tears should be mended or repaired. Before retiring, the interior should be searched for any mosquitoes or tears. It is a wise precaution to spray the inside with a pyrethrum space insecticide before getting under the net.

Today, all these suggestions are still valid. However, entomologists have long recognised that keeping a net in place is a problem. In fact, they even used bednets for sampling mosquito populations in the field (Lindsay & Gibson 1988).

4.1.1.2) Impact of untreated nets on malaria transmission

i) Effects on anophelines

In The Gambia, Port and Boreham (1982) used an experimental hut trial to study the effects of bed nets on feeding by An.gambiae in the field. They also made holes in the nets to simulate the usual condition. The results showed that

all the nets tested reduced mosquito feeding and this reduction inversely correlated with the number and size of holes in the nets. They also found that more unfed female anophelines left the huts with the nets than the hut with no net to seek for blood meals elsewhere. This suggested that bed nets were an effective means of reducing attacks by anophelines. Similar findings were also found by Charlwood (1986) in Papua New Guinea and Lindsay et al (1989) in The Gambia. In Tanzania, however, Lines et al (1987) simulated a badly torn net by cutting 8 holes of 10 x 20 cm. into it and found that it gave no more protection than without nets. Although the reduction of man-vector contact was shown, Port and Boreham (1982) found little impact of bed nets on malaria transmission especially in highly endemic areas. In these areas a high percentage of anophelines were infected and there was usually significant man-mosquito contact in the early part of the night prior to retiring. Lindsay et al (1989) reported that children under bednets still received more than one infective bite per year, suggesting that they were not effectively protected from malaria infection by sleeping under untreated bednets in The Gambia.

ii) Effects on disease

There have been a few records in the past on the effectiveness of bed nets in preventing malaria attacks mainly from military experience (Lindsay and Gibson, 1988). Recently, retrospective case-control studies in Columbia (Banguero, 1984) and Thailand (Butraporn et al, 1986; Fungladda et al, 1987) have shown that mosquito net users are significantly exposed to a lower risk of malaria attacks than non-users. An observational cohort study in The Gambia (Bradley et al, 1986) and an intervention study in Kenya (Nevill et al, 1988) showed similar results. However, longitudinal surveys of school children of a village of 1,000 in an area with perennial transmission in Congo, showed no significant differences between the malaria incidence rates in a bednet user group and those in a non-user group (Trape et al, 1987). Moreover, a randomised control intervention trial of bed nets by Snow et al (1988a) in The Gambia, which used a village as an intervention unit, showed that the risks to children age 1-9 years getting malaria attacks were not correlated with the use of bed nets. They concluded that bed nets were not effective in reducing malaria morbidity in this group of children because a significant number of them were found leaving their nets for a period during the night. The apparent protection

from bed nets demonstrated in previous retrospective studies might have been due to an increased number of infective bites being received by exposed individuals sleeping close to users of bed nets. These confirmed the previous entomological findings (Port and Boreham, 1982; Lindsay et al. 1989a). However, these findings cannot be generalised to the other areas which have lower levels of transmission.

In conclusion, untreated bednets may be useful for individual protection against malaria if properly used in low endemic areas, but at the same time, the malaria risk in non-users nearby may be simultaneously raised. On a larger scale, it is far from clear that they will give sufficient protection to a community. There are many reasons responsible for this failure (Curtis et al. 1990).

1. Nets may be torn or not properly used.

2. Mosquitoes may feed through nets on limbs which touch the nets during the night.

3. Mosquitoes may enter nets from underneath through slits in mattress supports which are made of woven string or maze stalks.

4. Users may be bitten before they go to bed.

5. Mosquitoes may be waiting around for their chance to obtain a blood meal when the users get out of the nets during the night.

4.1.2 Synthetic pyrethroids

A compound may be said to be a pyrethroid if its structure can be reasonably derived from that of natural "pyrethrins", and if it exhibits a range of biological properties that overlap to a considerable degree with those of existing members of the group. "Pyrethrins" are the active constituents of "pyrethrum extract". The term "pyrethrum" refers to the dried and powdered flower heads of Chrysanthemum cinerariaefolium. Solvent extraction of the flower heads yields a "pyrethrum extract".

The insecticidal activity of pyrethrum powder was known long before the nineteenth century. In 1924, the natural pyrethrins were extracted. It is known today that the insecticidal activity is due to the presence of six closely related esters of two cyclopropanecarboxylic acids in the natural pyrethrins. These acids are called chrysanthemic acids and pyrethric acids, and their six esters are called pyrethrin I, cinerin I, jasmolin I; and pyrethrin II, cinerin II and jasmolin II respectively (Davies,

1985). Pyrethrins are effective domestic insecticides that possess very low mammalian toxicity and used as models for the synthetic analogues (pyrethroids), insecticides of even greater efficacy and much wider application than their naturally occurring predecessors.

4.1.2.1 Development of synthetic pyrethroids

The first synthetic pyrethroid used in insect control was synthesised in 1949. This compound, named allethrin, was the ester derivative of chrysanthemic acid (Davies, 1985). After this discovery and up to about 1970 many other synthetic pyrethroids, such as bioallethrin, dimethrin, tatramethrin, resmethrin, bioresmethrin, prothrin were produced. Most of them were more potent than the natural product and also had lower mammalian toxicity. The most impressive one was bioresmethrin. It was an ester of 5-benzyl-3-furylmethyl alcohol; 4 times as active as parathion; and had a LD_{50} ratio of rat/housefly = 32,000 (Elliott, 1971). However, they were unstable in air and light. This property restricted their use to mainly domestic insecticides (Nishizawa, 1971). In 1973, Elliott et al reported that esters of 3-phenoxybenzyl alcohol were as potent as, but far more stable in light than bioresmethrin. This compound, named permethrin, opened the new era of photostable pyrethroid synthesis. Further studies by Elliott et al (1974) on variation of 3-phenoxybenzyl alcohols rendered esters of α-cyano-3- phenoxybenzyl alcohol. They showed an outstanding insecticidal activity especially a crystalline isomer, which was plainly 24 times and synergistically 45 times as active as bioresmethrin. It was called deltamethrin (or decamethrin before 1980). Cypermethrin was another photostable compound derived from α-cyano-phenoxybenzyl alcohol but less active than deltamethrin. Fenvalerate was the fourth of the photostable pyrethroids to be described from 1973 onwards, and was the first to be introduced into commerce in 1976 (Davies, 1985). The recent most potent photostable pyrethroids were fluorinated analogues of chrysanthemic acid. The most active compound, called cyhalothrin, was 2.5 times as active to the adult fly, Musca domestica, as deltamethrin (Bentley et al, 1980).

4.1.2.2 Mode of action and metabolism

All pyrethroids are lipophilic compounds, almost insoluble in water. These resemble those of the chlorinated hydrocarbon insecticides and differ

from most of the organophosphates and all carbamates. Most pyrethroids are relatively viscous liquids with high-boiling points and low vapour pressure. Only a few (eg. allethrin, prothrin and pyrethrin I) are sufficiently volatile to be useful constituents of mosquitoe coils (Elliott et al, 1978).

When lipophilic pyrethroid particles come into contact with an insect, they first passively penetrate through the cuticle to enter the haemolymph and are then carried to all parts of the body in solution, or bound to proteins, or dissolved in lipid particles. These result in neurotoxic symptoms before they are metabolised and excreted (Sun, 1968). The penetration can be faster with a lighter oily solvent of a pyrethroid and this will speed up the neurotoxic symptoms from it (Zerba, 1988).

In general, symptoms in an insect caused by pyrethroids are in two phases. The first is a phase of intense agitation and then, very rapidly followed by general paralysis. There are two possibilities in this latter phase: either the insect recovers after about 10 minutes (a 'knockdown' effect) or it dies (a 'killing' effect) (Hervé, 1982). Another effect is an irritancy/repellency effect which only drives an insect away without it being knocked down or killed. These effects depend on the compound concerned and the dose used (Quisenberry et al, 1984).

Narahashi (1971) reviewed studies on the mode of action of pyrethroids and concluded that pyrethroids caused hyper-excitation and blocking of nerves. He also reported that those occurred as a result of changes in nerve membrane permeability to sodium and potassium ions (sodium pump). Vijverberg et al (1982) also suggested the similar mode of action of the pyrethroids and DDT on the sodium pump in myelinated nerves and added that α-cyano substituted pyrethroids (deltamethrin, cypermethrin) caused more excitability than the non α-cyano substituted group (permethrin, phenothrin). This activity was also found inversely related to the temperature and the existence of the knockdown resistance (kdr) gene of insects. However, the detailed mode and sites of insecticidal and knockdown actions are still unclear (Miller and Salgado, 1985).

Insects have several enzymatic routes to metabolise and detoxify pyrethroids - primarily by oxidative and hydrolytic degradation. Esterases and mixed-function oxidases (MFOs) are the most important enzymes involved in pyrethroid metabolism (Leahey, 1985). The inhibitors of these enzymes may prolong

the stability and enhance the potency of pyrethroids - thereby serving as synergists, such as profenphos, piperonyl butoxide (PBO) and other organophosphorus inhibitors (Zerba, 1988).

4.1.2.3 Mammalian toxicity

Although pyrethroids are highly lipophilic, they are not stored to any significant extent in the fatty tissues, or any other tissues, of mammals (Leahey, 1985). In mammals, the most important metabolic process is cleavage of the central ester linkage. They are then hydroxylated and further oxidised. Most pyrethroid structures have numerous sites susceptible to attack by mixed-function oxidase systems. The addition of a cyanide group to the α-carbon of the pyrethroids, derived from 3-phenoxybenzyl alcohol, reduces the susceptibility of the molecule to both hydrolic and oxidative metabolism. For this reason, deltamethrin, cypermethrin and cyhalothrin are potentially the most metabolically stable. However, they are nevertheless sufficiently rapidly metabolised to allow efficient excretion by mammals (Soderlund & Casida, 1977: quoted in Leahey, 1985). This property is responsible for their lower mammalian toxicity compared to other classes of insecticides.

The signs of toxic action of pyrethroids in mammals are similar to those in insects (Litchfield, 1985). These can be divided into two neurological types. The first, caused by the non-α-cyano group (eg. allethrin, permethrin), are fine tremors progressing to whole body tremors and, with lethal doses, occasionally rigors just before death. These are similar to those of DDT. The α-cyano group (eg. cypermethrin, deltamethrin, cyhalothrin) produces abnormal exciting behaviour, profuse salvation, coarse tremor, abnormal hind limb gate, choreoathetosis and, with lethal doses, clonic seizures before death (Barnes & Verschoyle, 1974; Litchfield, 1985). Surviving animals appear to recover quickly and completely. Examination of nervous tissues showed that microscopic or ultrastructural changes occur only at lethal levels of pyrethroid administration and there is no evidence for changes at lower non-lethal doses. This may be explained by their high susceptibility to metabolic processes (Glomot, 1982; Litchfield, 1985). Pyrethroids cause none to moderate irritant effects on rabbit eye and skin. Permethrin elicited only minimal effects in the rabbit eye but did not show any indication of skin irritation. Cypermethrin, fenvalerate and deltamethrin had mildly irritant effects on rabbit eye but bioresmethrin

had no effect; and the former two were moderate skin irritants, whereas the latter had no effect (Worthing, 1979; Glomot, 1982). On long term feeding to rats, there has been no dramatic evidence of subchronic and chronic activity (Worthing, 1979). From the assessment of chemical structure and mutagenic assays, together with the overall lack of evidence shown by the long-term studies on several pyrethroids, it would appear that the pyrethroid molecule does not have carcinogenic properties (Litchfield, 1985).

Evidence of human toxicity is derived from the results of accidental or intentional poisoning, manufacturing practice and the normal use of the materials. One fatal poisoning, due to an accidental usage of cypermethrin formulation as cooking ingredient, has been documented (Poulos et al, 1982: quoted in Litchfield, 1985). Dermal effects on workers have been reported from deltamethrin manufacture prior to the installation of a new plant. This was observed as a pricking sensation initially and later developed into a blotchy erythema (FAO, 1982: quoted in Litchfield, 1985). In China, two thirds of workers engaged in packaging fenvalerate and deltamethrin developed burning sensations and numbness on their face and one third of them experienced sniffing and sneezing (He et al, 1988). The air concentration measured was 0.012-0.055 mg/m^3 for fenvalerate and 0.005-0.012 mg/m^3 for deltamethrin. No other abnormality or acute poisoning was observed. A study in volunteers showed that pyrethroids had little influence on neurogenic cutaneous vasodilatation on topical exposure (Flannigan & Tucker, 1985).

4.1.2.4 Ecological considerations

Non target organism may come into contact with an insecticide applied for a specific crop protection or public health purpose. This can be a direct contact at the site of an application or an indirect contact via air, water, soils or foods. Studies in birds revealed that they were less sensitive to pyrethroids than were mammals (Elliott et al, 1978; Hill, 1985). Bees, an important pollinator of wild and cultivated plants, especially honey bees, were found to be very sensitive to pyrethroids in laboratory conditions. However, in field studies, pyrethroids posed little or no hazard to bee populations following agricultural application. This was partly due to the low field application rates, partly to the repellency effects and also because the residues on plant surfaces showed a rapid fall in toxic effects to bees

(Lhoste & L'Hôtellier, 1982; Hill, 1985). Fishes were found to have about a 100 fold greater sensitivity to pyrethroids than mammals. This was probably due to the differences in both metabolism and physiological response (Hill, 1985). Fortunately studies in soils showed that the highly hydrophobic pyrethroids were virtually immobile and readily degraded within 1 day - 16 weeks, under aerobic condition. Thus they are highly unlikely to move from soils, the main point of entry, into any other parts of the general environment, including the aquatic environment (Leahey, 1985).

4.1.2.5 Use of pyrethroids in malaria control

A pyrethrum extract has been used for many decades as an aerosol for spray catching of anopheline mosquitoes in entomological studies. Before the discovery of DDT residual activity, it was used in trials to control malaria by frequent space spraying (Russel & Knipe, 1939). Though the result was good, the cost was too high so it was not suggested as a method for malaria control programmes. Since 1960, WHO has developed a scheme to screen and test insecticides for vector-borne disease control (WHO Pesticide Evaluation Scheme: WHOPES). The scheme clearly defines steps required for an insecticide to be recommended in a full-scale control programme (WHO, 1964; Wright, 1971; WHO, 1988a). More than 20 pyrethroids have so far been entered in the scheme including both photolabile and photostable groups. These pyrethroids were studied on their activities against both larva and adult anophelines of various species from laboratories and the field (Quélennec, 1988).

Early field trials of indoor-spraying of permethrin and deltamethrin showed the long residual effectiveness in reducing the number of house-resting anophelines (Rishikesh et al, 1979; Taylor et al, 1981). In 1984, Darriet et al reported an experimental hut study on the effects of bednets treated with permethrin at 0.08 g/m^2. They showed that the treated bednets were effective for about 4 months against An.gambiae and An.funestus even when they were torn. In 1985, Lines et al reported that curtains treated with permethrin at 0.2 g/m^2 also effectively reduce the number of anophelines entering houses. Since then, pyrethroid treated materials and their prospects for controlling malaria, have increasingly been the subject of many studies (Rozendaal, 1989; WHO, 1989; Curtis et al, 1990). These studies are

described in more details later in 4.1.3.

They are also used in mosquito coils and aerosol sprays against malaria vectors in some conditions. Pyrethrins and bioallethrin are used as a constituent in some brands of mosquito coils. Bioresmethrin, resmethrin, permethrin and deltamethrin are included in a recommended list for space sprays. They are widely used domestically, and are useful for application in tents and other enclosed areas as a temporary means of personal protection. This has no practical value in present day malaria vector control programmes, except in disinsection of international aircraft, ships and road transport. The space sprays of pyrethroids may be used outdoors against certain exophilic and exophagic vector species, and during malaria epidemics. Deltamethrin and permethrin (EC) are also recommended, with precautions, for larvae control (WHO, 1984; WHO, 1985).

4.1.2.6 Lambda-cyhalothrin

In 1980, Bentley et al reported a new fluorinated analogues of chrysanthemic acid in which the methyl groups, attached to the vinyl side-chain of the acid, were replaced by fluorine-containing alkyl groups. Among these analogues, most compounds had activities greater than permethrin and the most active one was the ester cyhalothrin, which was 2.5 times as active as deltamethrin. Cyhalothrin has sixteen different isomeric forms and the most attractive form from an economic standpoint is PP321 or lambda-cyhalothrin (Robson et al, 1984).

i) Physical and toxicological properties

Lambda-cyhalothrin is a white solid without any characteristic odour. It has a molecular weight of 449.9 and a melting point of 49.2 °C. Its vapour pressure is very low. It is hardly soluble in water but soluble in a range of common solvents. It is stable for at least 6 months at 15-25 °C (Jutsum et al, 1984).

Lambda-cyhalothrin is of moderate toxicity with oral LD_{50}'s to rats, similar to those of deltamethrin (Elliott, 1978; Jutsum et al, 1984). Lambda-cyhalothrin was highly active to a wide range of insects. It was 3 times as active as original cyhalothrin (Robson et al, 1984) and 7.5 times as active as deltamethrin to the adult house fly (Bentley et al, 1980; Robson et al, 1984).

ii) Biological evaluation

Field evaluations showed that lambda-cyhalothrin protected crops as good as or better than did cypermethrin and permethrin, with a 2-20 times lower dose (Jutsum et al. 1984). It has now been sold under the trade names of 'Karate' and 'Icon'. It proved to be safe to honey bees in the field evaluation following agricultural application (Gough & Wilkinson, 1984). Assessment of the impact on aquatic ecosystems showed that lambda-cyhalothrin was unlikely to cause adverse effects on populations or productivity in aquatic ecosystems when used for agricultural purposes (Berwick et al. 1984).

iii) Lambda-cyhalothrin and vector-borne disease control

Cyhalothrin has recently been classified in the WHO Recommended Classification of Pesticides by Hazards as class II:moderately hazardous, for tick control (WHO, 1988b). Lambda-cyhalothrin was included in the WHOPES scheme coded as OMS 3021. It has been tested in large-scale field trials against malaria vectors in Burma and Tanzania (Quélennec, 1988). It has been included in insecticide screening for impregnated nets against anopheline mosquitoes both in laboratory and experimental hut studies (Curtis et al. 1990; Miller et al. 1991; Lindsay et al. 1991). The results showed that a lambda-cyhalothrin impregnated net was more active than those impregnated with permethrin, deltamethrin and cypermethrin, with less deterrency effect than that treated with permethrin. After washing, nets treated with lambda-cyhalothrin and deltamethrin still rendered better insecticidal activities than permethrin-treated and untreated nets. Miller et al (1991) found that an actual dosage of lambda-cyhalothrin on the nets was only 2.6 mg/m^2 which was about 4 to 250 fold lower than those of deltamethrin and permethrin respectively. These finding suggested that a lambda-cyhalothrin impregnated net can be very useful for malaria control.

4.1.3 Pyrethroid treated bednets in malaria control

The idea of using chemical-treated bednets for personal protection against insects was independently developed during World War II. The Russians (Blagoveschensky et al. 1945) used repellents, while Americans (Harper et al. 1947) and Germans (Nauck et al. 1948) used DDT to treat nets against mosquitoes and

sandflies. After World War II, DDT was mainly utilised in the malaria eradication programme as an indoor residual spray. Alternative residual insecticides for indoor spraying were then developed and evaluated under the WHO Pesticides Evaluation Scheme (WHOPES) (Wright, 1971). In 1976, Brun and Sales evaluated nets impregnated with four different organophosphates but the results were not impressive. In 1973, Elliott et al reported an impressive activity of a photostable pyrethroid with low mammalian toxicity. Permethrin and deltamethrin were satisfactorily applied as indoor residual sprays in malaria control (Rishikesh et al, 1978). They were highly insecticidal, as well as excito-repellent. Permethrin was also used to treat clothes and jackets for personal protection against blackflies, mosquitoes (Lindsay & McAndless, 1978; Schreck et al, 1978) and ticks (Schreck et al, 1982). In 1983, WHO recommended field trials for photostable pyrethroid impregnated nets and many studies have since been reported around the world (Rozendaal, 1989; WHO, 1989; Curtis et al, 1990).

4.1.3.1 Technical aspects

i) Treatment of nets

Dipping of bednets into an emulsified solution of a pyrethroid is the method mostly used for treating nets. This can be done in two ways. The first is treating an individual bednet separately, by diluting the calculated amount of emulsified concentrated (EC) insecticide in the exact amount of water which would be required to just wet the whole net (Schreck & Self, 1985). The second is treating many bednets in the same time, by preparing a large amount of the emulsified solution. The solution concentration is calculated in the same way as the first. This procedure proved to be reliable and simple for both individual and mass treatments (Darriet et al, 1984; Lines et al, 1987; Snow et al, 1988b; Hossain et al, 1989). The wet net was then dried flat indoors on a bare mattress. This prevented breakdown of the pyrethroid by sunlight and allowed the surplus amount of the pyrethroid to soak into the mattress , which helped to kill bed bugs and may also prevent mosquitoes entering from below (Snow et al, 1988b; Lindsay et al, 1989b; Charlwood & Dagaro, 1989).

The other way of treatment is by spraying the insecticide on the nets (Loong et al, 1985; Yang et al, 1990). In the areas in which indoor residual

spraying is being operated, this method of treatment may be easily carried out by the malaria and vector control programme. The insecticide will be applied in the same way as is DDT in wall spraying. The advantages of spraying are quick application, safe handling of the insecticide, possibility for selective spraying and suitability for mass treatment (Lu, 1991). However, Rozendaal et al (1989) reported that cotton nets sprayed with permethrin were less effective than the nets treated by soaking at equivalent dosages.

Recently, an industrial treatment of nets at a manufacturing plant was considered as another possible way of mass impregnation. Nets may be better treated, last longer and the insecticides can be safely handled. However, the users in a village may not perceive the difference between an ordinary net and an impregnated net. This may make it more difficult for health education at village level (Rozendaal, 1989).

ii) Type of nets and materials

Synthetic nets treated with permethrin, deltamethrin and cyphenothrin (Hossain et al, 1989; Wu et al, 1991; Itoh and Kurihara, 1992) were far more toxic to tested anophelines than cotton nets. Hossain et al (1986) reported that scanning electron micrographs showed a smooth deposit of permethrin on nylon net material compared with an irregular deposit on a porous surface of a cotton material. This explained the bioassay findings. However, Wu et al (1991) reported that treated cotton bednets had a longer half-life than nylon. A study of the effect of insecticides, DDT, permethrin or deltamethrin, on tensile strength of both cotton and nylon netting (Li Zuzi et al, 1987; Wu et al, 1991) showed no signs of structural deterioration of the netting due to the insecticide.

iii) Wide mesh netting and torn bednets

The effectiveness of wide mesh netting, impregnated with an insecticide, depends on the wing span of mosquitoes and the period of time, they alight and pick up the insecticide on the net. These were studied by using inter-connecting laboratory cages with a piece of netting interposed between them. A bait was put in one side and mosquitoes were released into the other. For untreated netting, with 8 mm. mesh all mosquitoes alighted on the net, spent about 23 seconds resting on it and walked through (Itoh et al, 1986). With 16 mm. mesh only 6.3 % alighted on the

net and all flew straight through 32 mm. mesh netting. When netting was treated with phenothrin or fenitrothion, impregnated mesh of 6 - 10 mm. was effective in preventing feeding on the bait. Most anophelines were killed without having succeeded in passing through the netting.

With larger holes on a bednet, permethrin impregnation was shown to give an effective protection against anophelines in the experimental hut trials (Darriet et al. 1984; Lines et al. 1987; Carnevale et al. 1992). This suggests more effective use of nets in various conditions such as an easily damaged net, a net with entrance flaps, a hammock net and a wide mesh net.

iv) Residual activity

After impregnation of nets, their residual activity can be tested by using bioassay methods from which the results may be influenced by exposure-times, mosquito species, net materials, insecticides and their dosages. The exposure times in bioassay studies ranged from only 1 minute (Lines et al. 1987) to 1 hour (Darriet et al. 1984). Hossain et al (1989) found that double the exposure time resulted in mortality of less than double and suggested that the long exposure times were not sensitive for bioassay studies. This was confirmed by Rozendaal et al (1989). Culex quinquefasciatus is more tolerant than are anophelines (Hossain et al. 1989; Wu et al. 1991). Deltamethrin is more toxic than permethrin and both have better toxicity with higher dosages (Wu et al. 1991).

v) Durability

In general, pyrethroid treated bednets can be effective for several months. The durability of impregnated nets depends on chemical degradation; environmental factors like dust, smoke and weathering; handling, wrapping and washing of the nets. An un-used impregnated net seems to give a longer durability than one in use (Darriet et al. 1984; Loong et al. 1985; Lines et al. 1987; Li et al. 1987; Curtis & Lines, 1987). However, these results are not directly comparable due to the differences in methods used. Washing of a treated net can remove more than 50 % of the applied dose of various pyrethroids (Snow et al. 1987a; Curtis et al. 1990; Miller et al. 1991). The remaining toxicity depends on the amount of insecticides left on the washed nets (Rozendaal et al. 1989; Miller et al. 1991). Although these findings suggest that a durability of at least 6 months can be technically achieved

without difficulties, it can be too expensive in an area in which bednets are washed weekly, as in Suriname (Rozendaal et al, 1989).

vi) Behavioral studies

Behaviour of anophelines passing through wide mesh netting, studied by inter-connecting laboratory cages, have already been mentioned. In a more realistic condition, an observer sat under a net in a mosquito proof room into which An.gambiae were released (Hossain and Curtis, 1989). Mosquitoes were observed to remain standing and probing on the untreated net for considerably longer periods than on the permethrin treated net, confirming the excito-repellency effect of permethrin. With wide mesh netting or holes cut in a net, mosquitoes could enter into the net and a large proportion fed on the observer when the net was untreated. When the net was treated with permethrin fewer entered the net, only one fed, all were knocked down within 30 minutes and eventually died. To investigate whether mosquitoes could feed through treated netting, a tube containing mosquitoes were pressed against an arm interposed with a piece of permethrin impregnated netting. Results showed that even a dose as high as 2.5 gm/m^2 did not completely prevent feeding, though the fed mosquitoes died later. In the mosquito-proof room when an observer sat under the net and pressed his arm against the netting, released mosquitoes fed through the untreated netting but none did when the netting was treated with 0.2 gm permethrin/m^2.

4.1.3.2 Effects on the vector from experimental hut studies

Experimental hut studies with impregnated nets showed that impregnated mosquito nets had various effects in the field. These depended on net materials, insecticides and their dosages, type and condition of nets used.

i) Deterrency effect

Less mosquitoes entered the huts with pyrethroid impregnated nets than those without or with untreated nets (Darriet et al, 1984; Lines et al, 1987; Miller et al, 1991; Lindsay et al, 1991; Carnevale et al, 1992). Miller et al (1991) observed that permethrin treated nets gave more deterrency effect than other pyrethroids. Lindsay et al (1991) reported that the degree of deterrency was proportional to the dosage of permethrin. However, they found that this effect was

also caused by the blank formulation and therefore attributed it to other components of the formulation, rather than to the permethrin itself. Though permethrin has a low volatility, Ree (1988) found that it gave a fast vapour toxicity to caged anophelines hung around the treated net in an experimental hut, suggesting that this was due to an air-borne effect.

ii) Excito-repellency effect

After entering the huts, mosquitoes which left an experimental hut were trapped in exit traps. More anophelines exited the huts with permethrin impregnated nets than did those from the control huts, suggesting the excito-repellency effect of this pyrethroid (Darriet et al, 1984; Lines et al, 1987; Carnevale et al, 1992).

iii) Feeding success

Mosquitoes which entered the hut with impregnated net had lower engorgement rates than those which entered the control huts (with or without untreated nets) (Darriet et al, 1984; Lines et al, 1987; Miller et al, 1991; Lindsay et al, 1991).

iv) Killing effect

All studies found higher mortality rates in huts with pyrethroid treated bednets. Lambda-cyhalothrin and deltamethrin were more toxic than permethrin (Miller et al, 1991; Lindsay et al, 1991).

v) Mosquito nets with holes or opening

Permethrin impregnated bednets with large holes still gave effective deterrency, mortality and excito-repellency effects on anophelines as described more fully above, but to a slightly lesser extent (Darriet et al, 1984; Lines et al, 1987). The remaining effectiveness depends on the dosage of the insecticide on the torn bednets (Carnevale et al, 1992). A semi-closed treated bednet also gave similar results (Li Zuzi et al, 1987; Ree, 1988).

vi) Extended protection

Lines et al (1987) observed that in the presence of permethrin treated nets, mosquitoes showed a reduced tendency to feed on an unprotected person in the same room. Most of the mosquitoes which entered the room left without feeding. This may result from air-borne excito-repellency effects of permethrin.

4.1.3.3 Field studies on large scale trials

i) Problems of large scale field trials.

Evidences from laboratory and experimental hut studies indicate that nets treated with pyrethroids were effective in reducing bites from mosquitoes and killing them. The strong deterrency effect of permethrin makes it suitable for personal or household protection. The anophelines are forced to leave the house with treated bednets for blood meals in the neighbouring houses. This can result in more mosquitoes in the other unprotected houses and the overall transmission in the area may not be altered (Sexton et al, 1990). The community protection can be gained only when all, or a very large proportion of households use treated bednets (Snow et al, 1987b, 1988c). Deltamethrin and lambda-cyhalothrin are more toxic and less deterrent to mosquitoes than permethrin, therefore more mosquitoes enter but few survive, from the protected houses, to enter other unprotected houses. This killing effect can be enhanced (i.e. mass killing effect) by increasing the proportion of houses having treated bednets. This can introduce bias into comparison of the effects of impregnation in an intervention trial, if the treated and control groups are close together (Robert & Carnevale, 1991). The size and direction of bias depends on the insecticides used, the proximity of the intervention and control group and the feeding ranges of the vectors. The bias may be negligible if the protected proportion is very small compared to the unprotected controls (Snow et al, 1987b). However, an independent unit of intervention is preferred and more than one pair of comparison are needed for statistical analysis (Blum & Feachem, 1983; Kirkwood & Morrow, 1989; Bermejo & Veeken, 1992). Baseline data are also needed due to the high variability of malaria outcomes from year to year and village to village.

Therefore, the theoretically complete evaluation would involve a comparison between baseline and intervention periods and comparison between experimental and control groups (WHO, 1989; Molineaux, 1991). Moreover, the differences in the local epidemiological, ecological, sociocultural situations and methods used in many field trials cause difficulties in comparing results.

ii) Effects on anophelines

Reductions of indoor vector population were observed in all large scale intervention trials in Burkina Faso (Carnevale et al, 1988; Robert &

Carnevale, 1991), Tanzania (Magesa et al, 1991), the Gambia (Snow et al, 1987a; Lindsay et al, 1989c), Kenya (Sexton et al, 1990), Papua New Guinea (Charlwood & Graves, 1987) and China (Xu Jinjiang et al, 1988, Li Zuzi et al, 1989). A remarkable reduction in fed mosquitoes was also observed (Charlwood & Graves, 1987; Lindsay et al, 1989c). The exophilic and zoophilic An.sinensis in China was found to be significantly less affected by a village-scale intervention with deltamethrin-impregnated nets than An.anthropophagus (Li Zuzi et al, 1989). Snow et al (1987a) and Lindsay et al (1989c) found no significant difference between mortality rates of An.gambiae Giles s.l., caught in exit traps, from houses with permethrin-impregnated nets and those from houses with placebo-impregnated nets, although the exit rates from the former were significantly higher than those from the latter. A slight reduction of the outdoor vector population was found after spraying bednets with deltamethrin in Burkina Faso (Robert & Carnevale, 1991).

Various extents of reduction in survival rates after impregnation were observed in Papua New Guinea, Tanzania, Burkina Faso and China. Decreased sporozoite rates after intervention were observed in Burkina Faso, Tanzania and Papua New Guinea. These, together with the reduction of man-biting rates above, led to a considerable reduction in the estimated number of infective bites per person, indicating an impact of the intervention on vectorial capacities of those anophelines. A slight shifting of the feeding times towards earlier in the night was also observed in Papua New Guinea and Tanzania.

iii) Effects on the disease

In Thailand, Kamol-Ratanakul and Prasittisuk (1992) reported a randomise control trial using a migrant worker in an endemic village as an intervention unit. They found about 66% protective effects of the permethrin-treated bednets against malaria attacks in the village. In Kenya, Sexton et al (1990) used a household as an intervention unit for randomly allocating permethrin treated bednets, curtains and controls, after clearing all parasitemia cases with pyrimethamine/sulfadoxine. They found a significantly lower malaria incidence in the households with treated curtains and bednets compared with controls. However, these effects might be the result of risk deflection within the same village.

In the Gambia, Snow et al (1987b) treated only 10% of nets in a village and found that treatment of an individual's net gave a significant, but small effect. Among children aged 1-9 years under surveillance, only new febrile episodes with parasitemia were significantly decreased. No significant effect of individual use of permethrin impregnated nets was found on splenomegaly, packed cell volume or percentage of children with malaria parasites (parasite rates). However, in the later large scale, randomised control, village trials (Snow et al, 1988c), all the nets of certain villages were impregnated with permethrin 0.5 gm/m^2. The malaria morbidity of children aged 1-9 years in the intervention villages were compared with those in the control villages, in which all nets were impregnated with placebo. This was associated with significantly lower incidence of splenomegaly and less of a decline of packed cell volume than in the controls. Although the parasite prevalence rates were not significantly reduced, reductions in malaria attack rates, with any parasitemia and heavy parasitemia, were found to be 72% and 63%. This suggests that permethrin impregnated nets can effectively protect a whole community only when all nets in the village are treated (mass effect). In Burkina Faso (Carnevale et al: in Curtis et al, 1990), the village with deltamethrin-treated bednets significantly had less risk of malaria attack than the control village and no such effects found with parasitemia rate.

Nevertheless, in Papua New Guinea (Graves et al, 1987), there were only small significant reductions in the attack and prevalence rates of P.falciparum among children aged under 5 years in the intervention villages. Even worse was in Malaysia where intervention of nets treated with 0.062 gm permethrin/m^2 significantly reduced parasite rates for only 2 months after the distribution of the impregnated nets (Hii et al, 1987). These unsatisfactory results were partly caused by poor compliance of people who received the impregnated nets and the low level of the insecticide on the treated bednets. The social and ecological situations also played a higher role than the type of pyrethroids in Tanzania (Lyimo et al, 1991; Msuya and Curtis, 1991).

The impressive results come from China where there is a low endemicity. Li Zuzi et al (1989) carried out deltamethrin-impregnation net trials in a hilly region in which P.vivax was the only malaria parasite with an average monthly malaria incidence of 11.6% during July-December. The vectors were exophilic

An.sinensis (80%) and the endophilic and anthropophilic An.anthropophagus (20%). In the first trial in 1985 which involved 86.7% of the population in the study area, 1,855 bed nets were treated with 25 mg deltamethrin/m^2. This resulted in a 60.4% reduction of the monthly incidence. After the second intervention 10 month later, in which 2,457 bed nets (87.3% of the population) were treated, the average monthly incidence reductions were 74.6% and 92.7% as compared to the same periods in the pre-treatment year. Twelve months later, 24,665 bed nets, involving 83.6% of the whole district population (32,367), were treated in the same way. The average monthly incidence during April-December was reduced by 64.7% as compared with the corresponding period of the previous year. Control trials were conducted in another jungle and hilly region which had an annual malaria incidence rate of 40-110 per 1,000 persons, in spite of DDT spraying (Li Zuzi et al in: Curtis et al, 1990). An.dirus was the major vector in this region. In a treatment area of 6,407 population, 92.9% of all nets were treated with 25 mg deltamethrin/m^2. After the intervention the incidence was drastically reduced to 1.2 per 1,000 persons while the incidence in the control area slightly increased to 33.3 per 1,000 persons with untreated nets; and 33.4 per 1,000 persons without nets.

In other regions of China, the efficacy of permethrin-impregnated bed nets (200 mg/m^2), deltamethrin-impregnated bed nets (15 mg/m^2) and DDT spraying (2,000 mg/m^2) were compared with that in a control area (Li Zuzi & Lu Baolin: in Curtis et al, 1990). After the interventions, 85.7%, 87.4%, 20.5-92.0% and 40.5% reductions were found respectively. Although permethrin-impregnated bed nets and deltamethrin-impregnated bed nets rendered equally significant impact, the results were still in the range of DDT spraying efficacy.

The design of the Chinese studies are subject to many biases (WHO, 1989; Bermejo & Veeken, 1992). However, a remarkable reduction of malaria incidence after the intervention of the largest scale application in the world (more than 2 million bednets treated) (Curtis et al, 1990; Lu, 1991; Curtis, 1992), could not be totally explained by those biases.

The results of all trials suggest that the bednet impregnated with pyrethroids can be an effective measure for controlling malaria though it seems to have more effects on malaria fever than infection (parasitemia). Moreover, the most

interesting result is the reduction of the malaria-specific and overall mortality in Gambian children age 1-4 years after a large scale bednet impregnation programme through primary health care system (Alonso et al. 1991). This suggests that impregnated bednets can be an important simple measure against child mortality in an area of holoendemic malaria.

4.1.3.4 Safety consideration

Pyrethriods are highly toxic to an insect, with a very low mammalian toxicity and pose little effect on non-target organism and the environment in normal use. All photostable pyrethroids used in malaria control are classified by WHO as 'moderately hazardous' insecticides (WHO, 1988b). No serious side-effects after using permethrin treated nets were reported. WHO (1985) has accepted that properly treated bednets with permethrin should pose no hazard to those who use them. The alpha-cyano substituted group, such as deltamethrin and lambda-cyhalothrin, are far more active than permethrin but also have lower oral LD_{50}s in rats. They may cause eye irritation and skin paraesthesia. These were confirmed in the fields. Temporary paraesthesia has so far been noticed in China where the impregnation with deltamethrin was done by villagers without wearing gloves (Curtis et al. 1990). Lambda-cyhalothrin spraymen in Tanzania (Moretto, 1991) and Pakistan (Chester et al. 1992) reported temporary cutaneous sensory impairments, coughing, sneezing and eye irritation. These effects were reduced or stopped after washing with cold water. The similar side-effects were also found during dipping bednets with lambda-cyhalothrin and several days after using the dry treated bednets (Njunwa et al. 1991; Baskaran et al. 1991). All occurred with the dosage of 25 - 30 mg/m^2. The nose, throat and eye irritations were not considerably reduced when the dosage was reduced to 10 mg/m^2 or the newly treated bednets were hung unused for few days (Njunwa et al. 1991). Analysis of serum and urine after exposure by spraying or dipping found a very low level of insecticide metabolites without any changes in vital signs or liver function tests (Chester et al. 1992; Baskaran et al. 1992).

WHO (1985) accepted that pyrethroids had no harmful effects when applied at the recommended doses. Though the effect on people who handle concentrated products is minimal, it is a good practice to wear long water-proof gloves

and goggles while handling it. For a spray man, protective clothes must be worn. Hands and exposed skin must be washed thoroughly after using the concentrate.

4.1.4 Factors affecting a full-scale implementation programme

The different achievements in the large scale trials in different parts of the world suggest that a full-scale implementation of impregnated nets can be very complicated and requires more extensive interdisciplinary research. Many factors responsible for the effectiveness of the implementation should be studied at the beginning and the results should be used for guiding the implementation.

4.1.4.1 Local epidemiological conditions

The nature of malaria transmission in any single area is always different from others and should not be generalised (Molineaux et al. 1988). There are many factors related to malaria transmission. However, the major relation of the vectorial capacity and the prevalence of malaria have long been established (Ross, 1911) and several models of malaria transmission have been satisfactorily used to explain the different epidemiological conditions in different parts of the world (Molineaux, 1985). According to these transmission models, a large reduction of vectorial capacity in a holoendemic area needs to be achieved before the parasite prevalence starts to decrease. In a hypoendemic area, only a small reduction of the vectorial capacity will result in a considerable reduction of the parasite prevalence. These may partly explain the un-satisfactorily results in high endemic areas in Africa and Papua New Guinea, and impressive results in low endemic areas in China. However, Snow et al (1988c) suggested that, considering the long-term malaria control goals in highly endemic areas, the 63 - 72% efficacy achieved in The Gambia might be the most suitable level for that endemic area in which the natural immunity was still allowed to be built up by a lower number of infective bites.

4.1.4.2 Pyrethroid resistance

The principal resistance mechanisms of pyrethroids may include (Miller, 1988):

a) penetration resistance, where the composition of the insect's exoskeleton becomes modified in ways that inhibit pyrethroid penetration;

b) site-insensitivity, where the chemical site of action for a pyrethroid becomes modified to reduce sensitivity to the active pyrethroid form.

c) metabolic resistance, where the metabolic pathways of the insect becomes modified in ways that detoxify the pyrethroid.

d) behavioral resistance, where insect behaviour becomes modified so the insect no longer come into contact with the pyrethroid deposit;

Physiological resistance of anopheline mosquitoes to DDT and other classes of insecticides have been found in many areas. These are mainly caused by insect's knockdown-resistance (kdr) gene and multi-function oxidase enzymes (WHO, 1986). Pyrethroids posses similar mechanisms of action and resistance as does DDT. Cross-resistance of kdr type resistance between DDT and pyrethroids have been found in many species. This causes wide concern with the cross-resistance problem that may be anticipated when using pyrethroids in areas of DDT-resistant mosquitoes (Elliott et al, 1978; WHO, 1986). However, Malcolm (1988) recently reviewed the global situation of pyrethroid-resistance in anophelines and concluded that there was rather weak evidence of kdr-type resistance in anophelines reported around the world. An.stephensi was the only Anopheles so far in which there was strong evidence of this type of resistance. Chakravorthy and Kalyanasundaram (1992) found that An.stephensi selected by LD_{50} of permethrin for 5 generation resisted to permethrin, cypermethrin, alphamethrin and deltamethrin; and adding of synergistic chemicals (piperonyl butoxide) to permethrin, did not overcome the development of resistance. Organophosphate might be substituted for pyrethroids if resistance to the latter arises. Pyrethroids are detoxified by several esterases which are susceptible to inhibition by organophosphate and carbamate insecticides. Therefore, the use of pyrethroids mixed with these insecticide are reserved on toxicological grounds (WHO, 1989).

Another important mechanism of resistance is behavioral resistance. Several year after the implementation, shifting of biting times of the vectors from post-midnight to pre-midnight and biting habits from indoor to outdoor, could be expected (Charlwood & Grave, 1987). These are the same behavioral changes which were found after DDT house spraying (Ismail et al, 1975) and difficult to prevent. More infection may be contracted outdoor and outside the village. People may bring the impregnated nets with them and sleep under the nets when they stay

overnight outside the house to protect themselves from mosquito biting. This has been practised and found effective in rice-field huts in China with exophilic An.dirus (Li Zuzi & Lu Baolin: quoted in Curtis et al, 1990). However, in high transmission areas, other personal protection, such as repellents (Lindsay and Janneh, 1989), and vector control measures should be integrated (WHO, 1983).

4.1.4.3 Human factors

These are suspected to be the major factors responsible for the failures in large-scale intervention trials of untreated nets in The Gambia (Snow et al, 1988a) and impregnated nets in Malaysia (Hii et al, 1987). The villagers and children are not always in the nets when the vectors come to their houses. The mosquitoes usually have a chance to feed on these people before they retire or during the night when they get out of the nets for either indoor or outdoor activities. Moreover, they may even sleep outside the nets due to the uncomfortable hot climate. These problems may be partly related to the knowledge and perception of people about the risk of malaria and the proper use of bed nets; and partly related to intrahousehold cultural preferences. Other behaviours are related to the knowledge and perception of the additive effects of insecticides on the nets. In some areas, nets may be already widely used and it is common to have them washed frequently (MacCormack & Snow, 1986; Rozendaal et al, 1989). This has been proved to drastically reduce the efficacy of the impregnated nets. Health education therefore needs to be launched before or at the beginning of the implementation of impregnated bed nets. Before that, surveys of the sociocultural preferences of the local people of bednets and their use, are essential for understanding the community and achieving effective cooperation (MacCormack & Snow, 1986). These may also serve as an important guideline for improving the technical aspects of designing and treating nets to synchronise with the sociocultural conditions (Rozendaal et al, 1989).

4.1.4.4 Costs and affordability

In Tanzania, Njunwa et al (1991) found that the main obstacle to the widespread use of impregnated bednets is not acceptability but affordabilty. The costs of the programme largely depend on the local socioeconomic conditions. MacCormack et al (1988) studied the cost of various bednets in the local market of a village in the Gambia in 1987 and found that the estimated cost per year of a

permethrin-impregnated bednet was $2.05. The cost per year including the cost of chloroquine treatment, for a child over one year of age, was $1.05. The aggregate cost for each household could be $6.00 - $10.00 per year, depending on the family size. They further observed that an ethnic group which did not use bednets before could be convinced to use them and showed willingness to pay. It may be cheaper to import bednets in some circumstances but the use of local-made nets may be more preferable considering the long-term self-reliance goal.

In China, bednets are domestic products. After the initial successful interventions, impregnated bednets have been widely used in a full-scale control programme covering millions of people in endemic areas (Lu Baolin, 1991). The costs of this new implementation was estimated and compared with those of DDT house spraying. The cost of treatment with deltamethrin varied from about $0.05 in Sichuan Province to $0.10 per capita per year in Jiangsu Province. It was estimated to be about half to one-quater of the cost of DDT residual sprays and is about half the cost of permethrin treatment in Jiangsu Province in 1986.

4.1.5 Future research

The evidence from all the trials obviously confirm that impregnated bednets provide good personal protection against malaria by reducing man-vector contact. Trials to achieve a mass effect for community protection are not consistence in their results. However, they seemed to be more effective against malaria fever and death than parasitemia. Most of them were not comparable due to differences in the methodology, level of transmission, vector characteristics, the immune status and the socioeconomic conditions. These factors are area-specific Extrapolating the results from one area to another have to be done with caution. Further trials are clearly needed with much attention given to the method of community-intervention trials. Although strict guidelines are not possible due to the variability of trial setting, essential elements of community-intervention trials should be applied as rigorous as possible. Trials should include several communities, far enough apart to have separate vector populations. Intervention and control communities should be randomly selected and their comparability before the intervention should be provided. The outcome measures should be malaria morbidity or mortality. The results will be more comparable and useful for understanding how best to use the treated bednets as a

community-wide control measure (WHO, 1989; Bermejo & Veeken, 1992).

This thesis aims to study the mass effect of lambda-cyhalothrin treated bednets in forest fringe and hilly areas in the northwest of Thailand. This is the first study of this kind in Thailand.

4.2 Research questions and objectives

Can a community-wide bed net impregnation programme with lambda-cyhalothrin reduce the malaria morbidity in the forest border area in northwest Thailand. ?

4.2.1 Specific objective:

To measure the effectiveness of the community-wide lambda-cyhalothrin impregnation programme against malaria morbidity in this area.

4.2.2 Other objectives:

4.2.2.1 To describe the epidemiology of malaria morbidity in the area.

4.2.2.2 To describe the sociocultural aspects of the communities related to malaria illness and use of bednets.

4.2.2.3 To describe the sleeping patterns of villagers.

4.2.2.4 To measure the effectiveness of the community-wide untreated bednets programme against malaria morbidity

4.2.2.5 To measure the effectiveness of the impregnation programme against malaria prevalence.

4.2.2.6 To study the possible side-effects of the insecticide used.

4.2.2.6 To measure the compliance of the community on the community-wide programme.

4.3. Materials and methods

4.3.1 Study design

This is a randomised placebo control trial using a ban, the smallest community unit used by the malaria control programme in Thailand, as an intervention unit. The major outcome measure was malaria morbidity used by the control programme, the annual parasite incidence (API). It was collected one year before and 16 months after the intervention. The prevalence of malaria infection was also measured once a year during the rainy season to examine the possible effects of the programme on parasitemia. Studies on the general socio-cultural aspects related to malaria illness, use of bednets and sleeping patterns were carried out before the impregnation. Several cross-sectional surveys on the demographic data, use of bed nets, side-effects of the treated nets, compliance with impregnation and washing habits were also carried out before and after the impregnation.

4.3.2 Outcome measures

The annual incidence was defined as the number of malaria illness episodes per 1,000 persons at risk per year. The malaria illness was detected by the existing case detection systems. These comprised both active and passive case detection systems. The active system was carried out routinely by malaria workers who made a monthly round looking for malaria suspected cases. In the passive system, malaria suspected cases went to seek diagnosis and treatment from either malaria clinics or the primary health care services, ranging from malaria and village health volunteers to the district hospitals. The population at risk was estimated from the census surveys carried out during September to October each year.

The prevalence of malaria infection was defined as the proportion of positive blood slides from the mass blood surveys during October to November each year. The mass blood survey was aimed at taking blood slides from all villagers in the study area.

4.3.3 Sampling scheme and sample size

The routine case detection data from October 1988 to September 1989 were analysed to get an annual incidence rate in each ban in Mae Sariang district. There were 1,610 episodes detected from the total population of 61,099 in 305 bans. This is equivalent to the overall of 26.4 episodes/1,000 person-years. The annual rate

in each ban varied from 0 to 313 episodes/1,000 person-years. There were 94 (31%) and 56 (18%) bans with the rate higher than 30 and 50 episodes /1,000 person-years respectively (see Annex 2.1). The rates were transformed to a natural logarithmic scale to approximate the Normal Distribution. The sample sizes required to detect at least 50% effectiveness of the programme, with 95% precision and at least 80% power, were calculated based on the transformed rates. For achieving 90% power, 20 bans with the rate more than 50 episodes/1,000 person-years were needed. The size was increased to 26 bans with rates of more than 30 episodes/1,000 person-years with 80% power of detection (see Annex 2.2).

A list of bans in the district was used as a sampling frame; samples were surveyed and included as a pair. A total of 12 pairs were included under the following criteria:

1. They can be accessible throughout the year, at least by a motor cycle.

2. They have similar geographical characteristics subjectively assessed by the research team.

3. They belong to the same ethnic group.

4. They have a similar level of morbidity based on 1989 routine data.

5. Bans with an annual rate higher than 50 and 30 episodes/1,000 person-years were firstly and secondly considered respectively.

Three out of the 12 pairs were selected by an entomological research team led by Mr.Pradya Somboon for studying the entomological indices. The matching of these pairs was on the baseline entomological data. The other pairs were matched as mentioned.

4.3.4 Study period

The study was divided into 2 periods. The first was 12 months during February 1990 to January 1991, aimed at collecting baseline data. The second was 16 months during February 1991 to May 1992, aimed at collecting post-intervention data.

4.3.5 Distribution of bednets

Bednets were distributed through a community bednet fund. This is a community organisation handled by the community committee and supervised by a malaria worker. In 1989, several funds already existed and operated slowly in some

villages. Villagers were encouraged to donate a small amount of money to the fund. This money was used for buying bednets at a bargain price. Villagers may buy bednets from the fund and pay the cost in increments over a certain period. Extended credit was given to poor members of the community who might never be able to afford a bednet. The research team encouraged every ban to set up its own fund. Villagers did not need to donate money for the new fund. All bednets required by villagers were donated to the fund by the research team and villagers bought these bednets from the fund at a subsidised price. The money in each fund was raised in this way and the ban committee was responsible for managing the fund aimed to sustain the availability of bednets for each ban. Villagers were also encouraged to acquire enough bednets for their use both within the residence and during moving. They could order bednets of any size appropriate to their own use (see Annex 2.3).

Six pairs of bans were randomly allocated bednets they required, in May 1990. In February 1991, bednets were distributed again to the other six pairs and also the previous ones which required a few more bednets. This aimed at creating an imbalance of bednets in the study bans during the first period, to allow for measuring the effects of untreated bednets.

4.3.6 The impregnation programme

4.3.6.1 Intervention and control

The intervention was the lambda-cyhalothrin impregnation programme. Villagers in the intervention ban were encouraged to bring their bednets to be dipped in the aqueous insecticide solution by the research team and malaria workers. There were 2 rounds of impregnation, during February to March 1991 and October to November 1991.

The control was the placebo impregnation programme. Villagers in the control ban received the same encouragement as in the intervention ban.

The placebo was a white water colour concentrated solution. It was contained in a bottle with the same appearance and labels as the concentrated insecticide solution.

4.3.6.2 Impregnation process

The mass dipping process was developed in a laboratory room and tested in the pilot area in December 1989 (see Annex 2.4). Under the process,

a bednet was dipped in an insecticide or placebo solution, wrung and hung up on a rope to allow the excess solution to drip for about 5 minutes and wrung again before putting in a bag and given to its owner to be dried at home.

4.3.6.3 Dosages

The target dosage was 10 mg/m^2 of lambda-cyhalothrin. The actual dosages on the treated nets dipped in the insecticide solution with different concentration was unclear (see Annex 2.4) and there was not enough time to repeat the study. However, the bioassay test suggested that the dipping method and concentration used in the pilot area gave at least 6 months effectiveness (see Annex 2.4). Three dosages were deliberately used in the study area. There were two reasons for this. The first was to allow for the best and worst possibilities, based on the actual dosage study results, with minimum chance of possible harmful side-effects. The second was to see the possible dose-response side-effects of the treated bednets. The three concentration were based on the three different aqueous dilutions of 5% emulsified concentrated solution of lambda-cyhalothrin, 100, 200 and 300 times dilution. The 100 times dilution was chosen by the entomological study team to implement in three pairs of bans under their entomological surveillance. The other dilutions were randomly allocated to the other pairs of bans using a block randomisation method. In each pair, the placebo solution was also diluted in the same fashion.

However, the 300 dilution factor was used in all bans during the second impregnation. This was due to the complaint of many villagers on the side-effects of the higher aqueous concentrations during the few weeks after the first impregnation.

4.3.7 Allocation of the intervention

The decision for allocating the insecticide solution in the three pairs was done by the entomological team. Among the other pairs, the allocation was done by the block randomisation method.

4.3.8 Other control measures

The other control measures were routinely applied except DDT household spraying. The operation was stopped in the study bans. The last round of DDT spraying was in October 1989.

4.3.9 Data collection

4.3.9.1 First year data collection: before intervention.

The first census survey was done during January -March 1990. This included questions on a number of household members, age, sex, the amount and sizes of bednets possessed, bednet usage during the previous night and the amounts and sizes of new bednets which need to be bought from the bednet fund. The total amount and sizes of bednets needed were prepared and distributed to the bednet funds in May. At the time of the distribution, 30% of all households were randomly selected for structured questionnaire interviews on the socio-cultural aspects of malaria illness and use of bednets. The census survey was repeated during September - November 1990 with the same questions. The amount and sizes of new bednets ordered were prepared and distributed at the beginning of the second phase in February. The population data was also used as an estimate of the mid-year population at risk prior to the intervention.

During August to November, 11 households in 2 bans were randomly selected for a small scale observational study on the sleeping patterns of villagers. One research assistant and one interpreter stayed in each household for 4 pairs of nights. The sleeping times, use of bednets and activities outside the bednets were directly observed and recorded in a form designed by the social scientist.

Mass blood surveys were carried out in all bans during October to November 1990. Both active and passive case detection were operated as usual. The names and addresses of cases were cross-checked with the census data to confirm the accuracy of the addresses.

4.3.9.2 Second year data collection: after intervention.

The number of bednets in each household brought for each impregnation were recorded. In the first impregnation, a water soluble ink was marked on all treated bednets in one village after they were dried. This aimed to assess the washing habit of villagers. The previous 30% household samples were surveyed again with a structured questionnaire on the side-effects of any members in the households.

A third census survey was carried out during September - October 1991 to get the mid-year estimate of the population at risk after the

intervention. Questions were also added on the use of bednet during the night before, whether the bednets were washed and when.

The mass blood surveys were again carried out in all bans during October - November 1991. The case detection systems were operated and the names and addresses of cases were cross-checked with the census data as previously mentioned.

4.3.10 Data analysis

Proportions (%) were used to described the social characteristics, use of bednets, sleeping patterns, coverage, washing rates and other data, including the prevalence of infection. The chi-square method was used for analysis. The incidence rate was calculated by dividing the number of malaria episodes with the mid-year population at risk. The rate in each ban was adjusted by age and sex, using the total population in 24 bans as the standard population (Armitage and Berry, 1987). The rate ratio in each pair of bans was calculated using the rate in the ban receiving placebo as a reference category. The ratios were transformed to the natural logarithmic scale and the means and standard errors were calculated on the transformed scale using the t-distribution values. The results were converted back to get an average rate ratio and its 95% confidence interval. The incidence rate ratios were calculated for the data 12 months before the intervention, 8 months after the first and 8 months after the second impregnation. Each incidence and prevalence rate was added by 1 to allow for successful transformation.

4.4 Results

4.4.1 Descriptive results

4.4.1.1 Demographic characteristics

A total of 24 bans were included, matched and randomised according to the plan. Table 4.1 shows details of each ban prior to the study. The

Table 4.1 Details of the 24 bans prior to the study.

Pair no.	Ban[1] no.	Situation[2]	Ethnic group	Population[3]	Annual malaria[3] incidence rate
01	01	Forest fringe	Karen	400	35.0
	02	Forest fringe	Karen	192	36.5
02	03	Forest fringe	Karen	226	61.9
	04	Forest fringe	Karen	431	55.7
03	05	Riverside	Mix	148	81.1
	09	Riverside	Mix	81	61.7
04[4]	07	Forest fringe	Karen	459	74.1
	15	Forest fringe	Karen	261	149.1
05[4]	08	Forest fringe	Karen	719	80.7
	16	Forest fringe	Karen	90	144.4
06	06	Plain	Thai	210	109.5
	10	Plain	Thai	97	103.1
07	11	Forest, hilly	Karen	57	122.8
	12	Forest, hilly	Karen	199	100.5
08	17	Forest fringe	Karen	58	275.9
	18	Forest fringe	Karen	95	189.5
09[4]	19	Forest, stream	Karen	116	241.4
	25	Forest, stream	Karen	118	279.7
10	20	Forest fringe	Karen	261	42.1
	23	Forest fringe	Karen	n.a.	n.a.
11	21	Forest, hilly	Karen	45	333.3
	22	Forest, hilly	Karen	49	204.4
12	13	Forest, hilly	Karen	70	100.0
	24	Forest, hilly	Karen	157	57.3

1 - Bans were numbered in the order of pre-study survey. Bans number 14 and 26 were excluded because they were too small.
2 - All bans were visited before being included and their geographical situations were used for matching.
3 - Source from routine data collection by malaria sectors.
4 - These pairs were selected by the entomological research team for evaluating entomological indices.

Table 4.2 Age and sex structure from the second population survey during September - November 1990.

Age (year)	Male (%)	Female (%)	Total
0- 9	609 (52)	566 (48)	1,175
10-19	558 (52)	510 (48)	1,068
20-29	455 (51)	442 (49)	897
30-39	316 (53)	278 (47)	594
40-49	191 (50)	192 (50)	383
50-59	155 (51)	149 (49)	304
60+	152 (53)	137 (47)	289
unknown	1		1
Total	2,437 (52)	2,274 (48)	4,711

total population as 4,624, 4,711 and 4,715 persons were from the first, second and third census surveys during January-March 1990, September-November 1990 and September-October 1991 respectively. Table 4.2 shows the age and sex structure of the study population.

4.4.1.2 Epidemiological characteristics

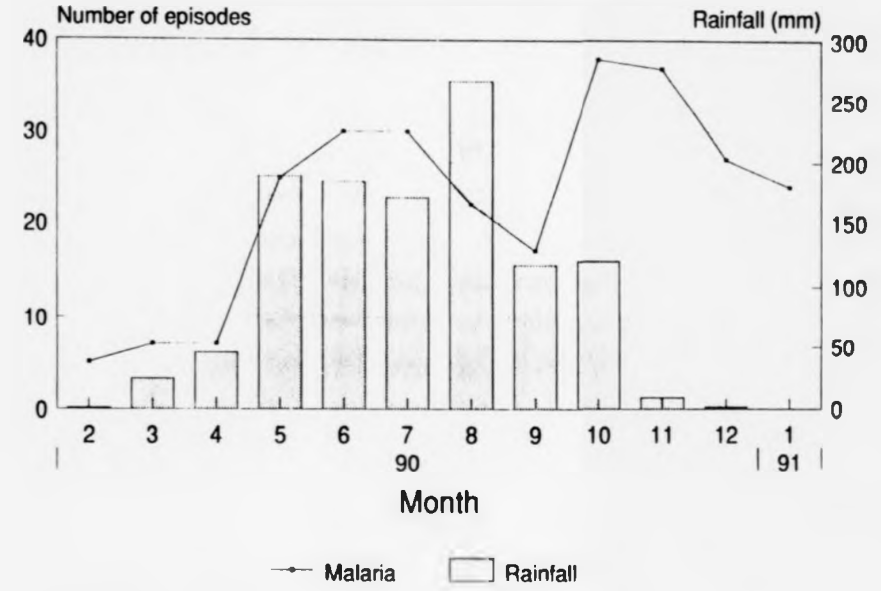
i) Incidence of malaria illness

A total of 267 malaria episodes were detected during February 1990 to January 1991. The annual incidence rate is estimated to be 56.68 episodes/1,000 persons. Episodes in the same person, less than one month apart, were included only once. Only 30 episodes (11.2%) were detected by active case detection system. Most patients went to malaria clinics (46.1%) or district hospitals (33.0%) for rapid diagnosis and treatment. Only 2.6% and 6.4% were detected by malaria volunteers or health posts, respectively.

a) Seasonality

Figure 4.1 shows a bimodal variation of incidence cases. The first peak is during June and July and the second is in October. The second is higher than the first one. It was increasing when the amount of rainfall was decreasing, suggesting different transmission dynamics from the first peak.

Figure 4.1 Seasonality of malaria incidence and rainfall.



Mae Sariang, Thailand.

b) Type of infection

The majority (89.9%) of cases were infected with P.falciparum malaria. The rest were infected with P.vivax malaria. There were no cases infected with other types of malaria parasites.

c) Age- and sex-specific incidence

Figure 4.2 shows age- and sex-specific incidence. Males significantly predominate in all age groups except among children of 0-9 years. Young adult males of 20-39 years of age carry the highest risk.

ii) Prevalence of infection

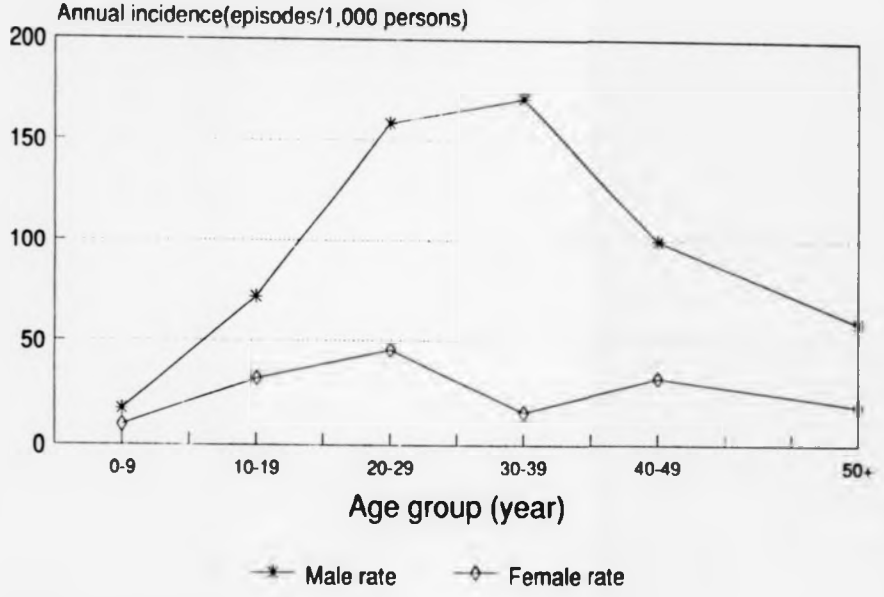
During October to November 1990, a total of 2,755 (63.4%) persons had blood slides taken in the 22 bans. Only 51 slides (1.85%) were found positive for malaria parasites. Table 4.3 shows the proportion of blood slides during the survey. Adult males were under covered, this is because they have high rates of movement, as shown in the previous chapter. Hence, the results of mass blood surveys are likely to reflect more the prevalence of infection within, than outside the village. Figure 4.3 shows age- and sex-specific prevalence. The rates are similar in all age groups and sexes. The predominance of adult males, seen in the incidence analysis, disappears.

Table 4.3 Coverage of mass blood survey by age and sex[1].

Age (year)	Male			Female			Total		
	Total	Covered	(%)	Total	Covered	(%)	Total	Covered	(%)
0- 9	573	412	(72)	514	379	(74)	1,087	791	(73)
10-19	506	303	(60)	471	320	(68)	977	623	(64)
20-29	419	207	(49)	411	282	(69)	830	489	(59)
30-59	607	344	(57)	576	360	(63)	1,183	704	(60)
60+	143	75	(52)	126	73	(58)	269	148	(55)
unk.	1	-	-	-	-	-	1	-	-
Total	2,249	1,341	(60)	2,098	1,414	(67)	4,347	2,755	(63)

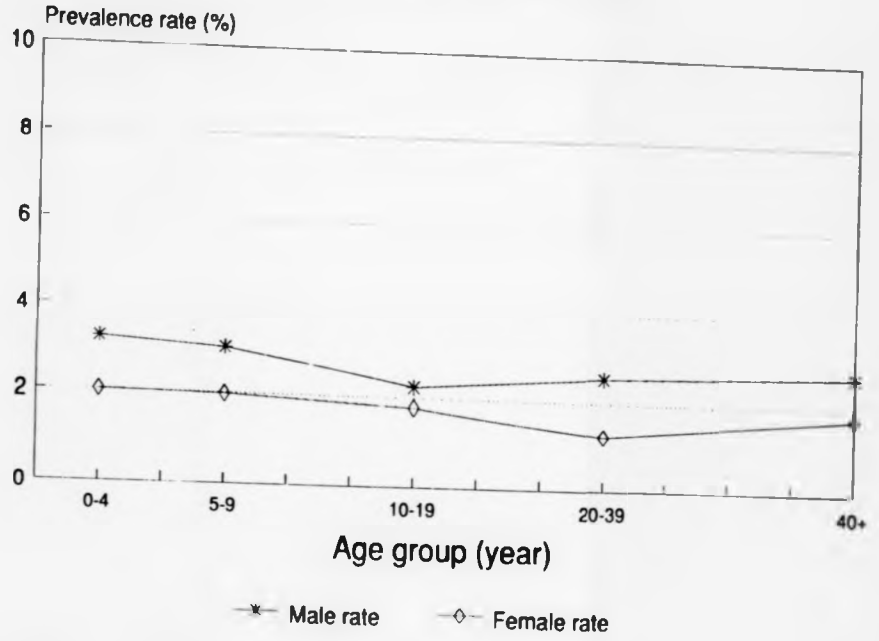
1 - From the first mass blood survey during October to November 1990.

Figure 4.2 Annual incidence rate, by age and sex.



Mae Sariang, Thailand, Feb'90-Jan'91.

Figure 4.3 Prevalence rate, by age & sex



Mae Sariang, Thailand, Oct-Nov'91.

4.4.1.3 Use of untreated bednet

i) Number, size and material

The first census survey during January to March 1990 revealed that most households already possessed bednets. The total number of bednets was 1,596. The average number of persons/bednet was 2.9. After the first and second distribution of bednets, numbers of bednets increased to 2,251 and 2,606 in 1990 and 1991 respectively (Table 4.4). The number of persons /bednet decreased to 2.1 and 1.8 respectively.

Table 4.4 Number, size and material of bednets.

Period of survey	Type of net	Size			Total (%)
		Small	Medium	Large	
Jan-Mar[1] 1990	Cotton or polycotton	466	598	386	1,450 (91)
	Nylon	26	72	48	146 (9)
	Total (%)	492 (31)	670 (42)	434 (27)	1,596
Sept-Nov[2] 1990	Cotton or polycotton	686	658	532	1,876 (83)
	Nylon	77	199	99	375 (17)
	Total (%)	763 (34)	857 (38)	631 (28)	2,251
Sept-Oct[3] 1991	Cotton or polycotton	857	690	827	2,374 (91)
	Nylon	94	81	57	232 (9)
	Total (%)	951 (36)	771 (30)	884 (34)	2,606

1 - A total of 1,015 households contained 4,624 members. There was no record on bednet details in 19 households (63 members).

2 - A total of 1,032 households contained 4,711 members.

3 - A total of 1,043 households contained 4,715 members. There was no records on 2 households (5 members) and 30 bednets were of unknown sizes.

Only 9% of the existing bednets were nylon. Cheap nylon bednets were bought from a bednet company in Thailand and sold through the bednet fund scheme at a subsidised price. This made the proportion of nylon bednets considerably greater during the second survey. However, these nylon bednets were easily torn in the conditions of the Karen households. Therefore, most of them were badly torn in a later year. Most of the remaining nylon bednets were stronger and more expensive. They were bought independently from markets.

ii) Prevalence of bednet use

During the census surveys, a question was asked on whether a household member slept under a bednet the night before each survey. The answers were 'yes', 'no' or 'not known, due to absence'. The latter were excluded from the analysis of prevalence of bednet use. The resulting prevalence reflects the cross-sectional view of how bednets were used in the village. The prevalence of bednet use were 61%, 86% and 94% during the dry and late rainy seasons of 1990 and 1991 respectively. Table 4.5 shows the prevalence of bednet use by age, sex and the availability of bednet in each household from the census surveys. Males, people of 10-19 and more than 59 years of age consistently used bednets less than the others. The number of bednets available in each household was significantly related to the prevalence of bednet use ($p<0.00001$ by chi-square test for a trend). The latter finding suggests that the main obstacle to the use of bednets is availability to the villagers. When the availability subsequently increased, due to the distribution of bednets before each census survey, the prevalence of bednet use also increased ($p<0.00001$). However, the absolute prevalence rates could be overestimated because villagers would tend to please interviewers. In households with no nets, the rates of 0 - 6% prevalence may reflect the approximate size of this over-estimation.

Table 4.5 Prevalence (%) of bednet use in each survey.

a) Prevalence by age group

Age group (year)	Jan-Mar'90[1] % (Total)	Sept-Nov'90[2] % (Total)	Sept-Oct'91[3] % (Total)
0 - 9	64 (988)	88 (1,116)	96 (1,113)
10 - 19	55 (945)	83 (987)	92 (920)
20 - 29	66 (727)	87 (832)	95 (829)
30 - 59	63 (1,163)	86 (1,210)	95 (1,222)
60+	55 (275)	79 (271)	90 (298)
Total	61 (4,098)	86 (4,416)	94 (4,379)

b) Prevalence by sex

Sex	Jan-Mar'90[1] % (Total)	Sept-Nov'90[2] % (Total)	Sept-Oct'91[3] % (Total)
Male	58 (2,109)	84 (2,252)	93 (2,214)
Female	64 (1,989)	88 (2,164)	95 (2,168)

c) Prevalence by availability of bednet in each household.

Number of nets/member	Jan-Mar'90[1] % (Total)	Sept-Nov'90[2] % (Total)	Sept-Oct'91[3] % (Total)
0.0	3 (630)	6 (296)	0 (54)
0.1	32 (427)	55 (281)	58 (98)
0.2	65 (850)	86 (660)	90 (551)
0.3	76 (537)	94 (543)	96 (528)
0.4	83 (474)	96 (502)	98 (490)
0.5	83 (509)	95 (856)	96 (934)
0.6	87 (286)	97 (564)	98 (714)
≥0.7	85 (385)	96 (714)	99 (1,010)

1 - No records for 526 persons.
2 - No records for 295 persons.
3 - No records for 333 persons.

iii) Social surveys on malaria illness and bednet use

These were structured questionnaire interviews of 279 households randomly selected from the total households in the study area, in May and December 1990. The heads of household were interviewed about their knowledge, attitudes and behaviour of malaria illness and the use of bednets.

a) Knowledge and attitude to malaria illness

a.1 Severity of malaria illness

About 83% agreed that malaria illness could cause death.

a.2 Causes of malaria illness

Mosquito biting	58%
Sleeping in the forest, drinking water from a stream	5%
Not known	36%

a.3 Malaria symptoms

Chill	79%
Headache	63%
Fever	37%
Nausea, vomiting	26%
Intermittent fever	22%
Dizziness	22%
Yellow skin	12%

a.4 Experience of malaria illness

Never 75%

Yes 25% - Place of infection

In the village	25%
Farm, stream	26%
Forest	26%
Forest in Myanmar	17%
Not known	5%

b) Use of bednets

b.1 Experience of using a bednet

Never 7.5%

Yes 92.5% - When was the first use.?

Adulthood	75%
Childhood	25%

b.2 What are the advantages of sleeping under a net?.

Preventing mosquito biting	85%
Preventing malaria illness	5%
Preventing other insects	2%
Others	8%

b.3 Reasons for first use

Preventing mosquito biting	56%
Following parents' use	17%
Following others' suggestions	13%
Preventing small insect biting	4%
Others	10%

b.4 Preventive measures before the first use

Sleeping besides a fire	37%
Covering with a blanket	34%
None	29%

b.5 Availability of bednets

Not enough	24%
Just enough	60%
Having unused bednets for guests	16%

b.6 Any overnight guests during the last rainy season

No 51%

Yes 49% - The guests slept under a net?.

No 69%

Yes 31%

b.7 Net material preferred

Nylon 13% - Reasons were cool, comfortable, beautiful color, easy to wash and cheap.

Cotton 83% - Reasons were last longer and more effective in preventing small insect biting.

b.8 Frequency of washing a bednet, last year

Never wash	7%
Once	15%
Twice	41%
More than twice a year	37%

- Reasons were dusty, heavy contamination by infant defecation and urination.

c) Use of bednets in farm huts

Households without farm huts	32%
Households with farm huts	68%

For households with farm huts

c.1 Distance from the village

Within 2 km.	65%
Further than 2 km.	35%

c.2 Hut materials

Almost all huts were made of bamboo.

c.3 Use mattresses

Yes	77%
No	23%

c.4 Use of bednets at the farm huts

No bednets	27%
Taking bednets from home and bringing back	61%
Having bednets at the huts permanently	12%

c.5 Activities during the dusk

Within the huts	50%
Both within and outside	50%

c.6 Activities during the dawn

Within the huts	67%
Out of the huts	33%

iv) Size and use of bednets

A question on the place that bednets were used, was added to the third census survey during September to October 1991, when all bans had enough bednets. Table 4.6 shows that when it is affordable, a household prepares bednets for 3 main purposes, using them in the household (73%), keeping some of them for guests or later use (19%), and keeping some of them in the farm hut for regular use away from the household (8%). The second proportion (19%) is higher than that from the previous survey (16%) (see 1.3.3.b.5 above). The third proportion (8%) is the same as before (see 1.3.3.c.4; 68% of all households had farm huts and 12% of farm huts

having bednets kept them in permanently, 12% out of 68% is equal to 8.2%). The bednets for the second purpose were mostly of the small size (70%).

Table 4.6 Size of bednets by place of use.

Place of use	Size of bednet			Total (%)
	Small (%)	Medium (%)	Large (%)	
In the household	569 (30)	567 (30)	736 (39)	1,872 (73)
In the farm hut	137 (70)	40 (20)	20 (10)	197 (8)
Keep in reserve	233 (47)	145 (29)	117 (24)	495 (19)
Total	939	752	873	2,564 (100)

N.B. - Seventy two bednets with incomplete records were excluded.

4.4.1.4 Sleeping patterns

During August to November 1990, 2 bans were selected for a small-scale observational study. These were ban no.15 and 25. The total number of households were 57 and 23, bednets were 135 and 25, and the average number of persons per each bednet were 2.0 and 4.4, respectively. Six and 5 households were randomly selected from these bans. A research assistant and an interpreter stayed overnight within each household for 2 consecutive nights in each month, for 4 months. The observers brought and used their own bednets. They slept in common parts of the household to avoid the disturbance caused to the sleeping habits of the household members. Apart from the observation schedules, the observers also visited the bans from time to time for other research purposes. The household members had a good relationship with the observers. However, to minimise the possible bias from the introduction of the observers into the households, only 259 person-nights records from the last 2 months were analysed.

i) General observations

Ban no.25 was located in a forest hilly area, with difficult access and not enough bednets. The household in this ban had separate bedrooms. However, during the observation period, household members did not use the bedrooms. They slept in the kitchen. The Karens had this habit as a part of their way of life. This is because they had no bednets and a fire in the kitchen was used both for warming and preventing mosquito bites. Ban no.15 was located lower in the forest fringe area and more accessible. It had a bednet fund and had just received bednets from the research team in May 1990, before the observation. The household members slept in separate bedrooms. An infant slept under the same bednet with its parents. Young children used the same bednet. Single young adults of the same sex used the same large- or medium-sized bednet. A married couple had a separate bedroom. All Karen houses had the same characteristics. They were raised from the ground on stilts and had overhanging eaves. The material of the houses depended on the household socio-economic status. They ranged from small bamboo houses with thatched roofs, to larger wooden houses with corrugated iron roofs.

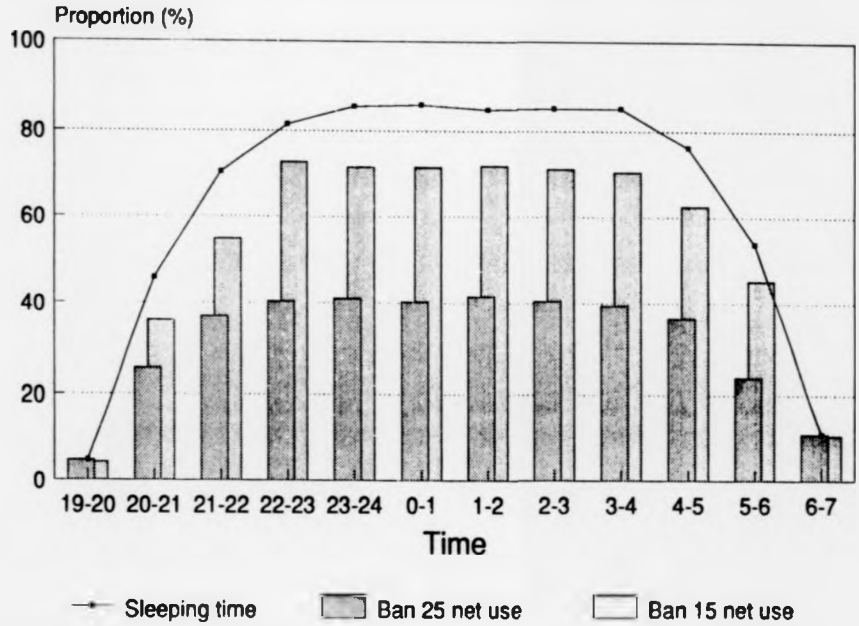
ii) Sleeping time and use of bednet

Figure 4.4 shows the sleeping time of household members in both bans. About 86% of the total household members were staying in the household (see Annex 2.5). Most of them went to bed after 21.00 and got up after 6.00. The use of bednets in Ban 15 was significantly higher than in Ban 25 ($p<0.05$). This suggests that the use of bednets can be increased by improving the affordability of them. Figure 4.5 shows that young people of 10-29 years go to bed the latest and sleep least under bednets. Males go to bed later and sleep less under bednets than female (Figure 4.6) but these are not statistically significant.

iii) Activities outside bednets

There were many reasons keeping people outside bednets during the night time. With about 10% of the total person-nights people went away from the ban and did not come back to sleep during the night. Most of the reasons were for visiting friends or attending traditional festival in other bans, when they stayed overnight with their friends and returned to the household in the morning. Among the others who stayed in the household, there were many reasons keeping them outside

Figure 4.4 Sleeping time & use of bednet



Mae Sariang, Thailand, Oct-Nov'90.

Figure 4.5 Sleeping time and use of bednets, by age group.

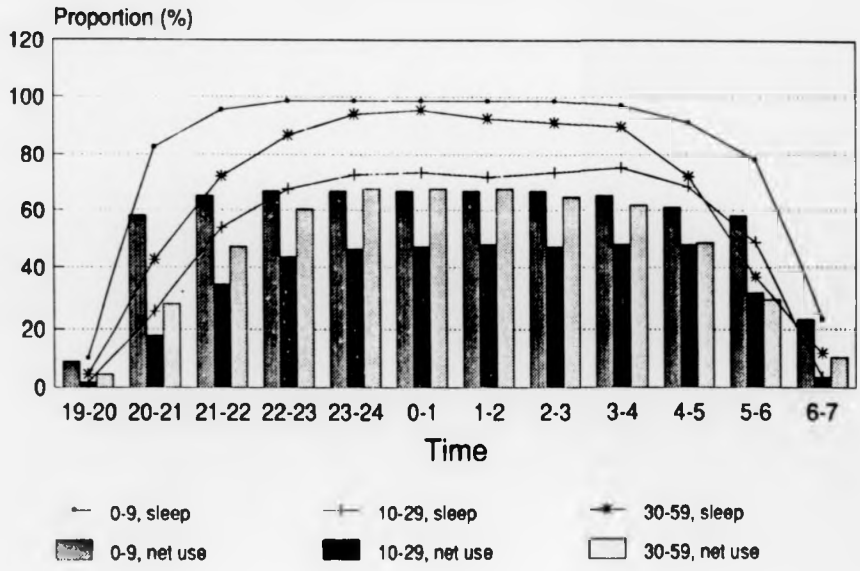


Figure 4.6 Sleeping time and use of bednets, by sex.

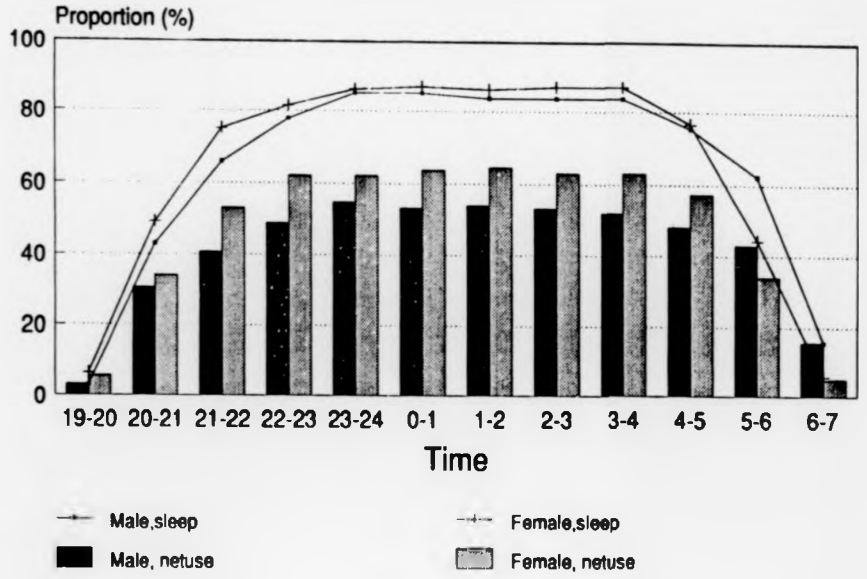
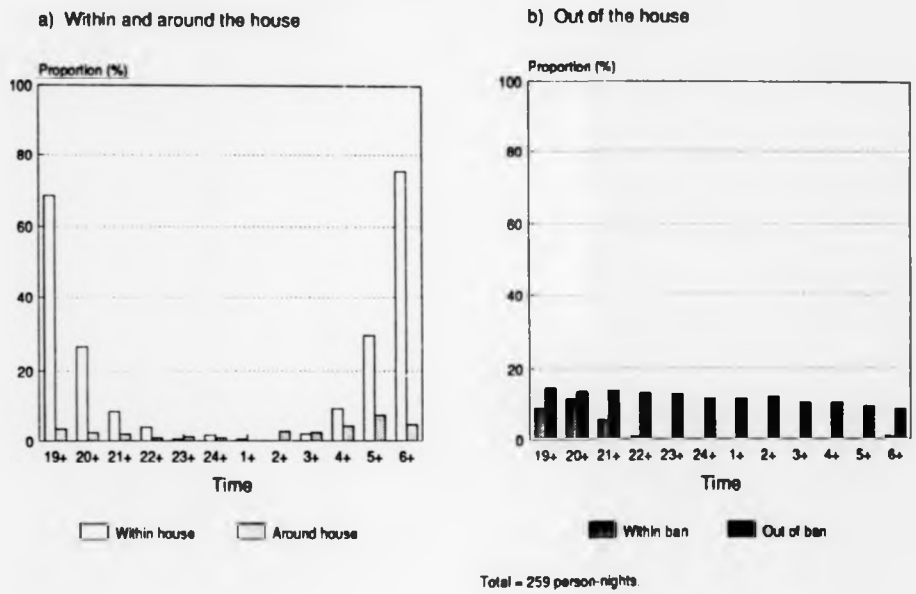


Figure 4.7 Activities outside a bednet.



bednets. Figure 4.7 shows that most activities outside a bednet were carried out within the household, both before retiring at night and after getting up in the morning (see Annex 2.6). Before going to bed, these were cooking, having meals, studying, chatting and watching television (if any). After getting up during the dawn, these were cooking, having meals and small household jobs.

iv) Validity of bednet use

The prevalence of bednet use in each ban, gained from the second census survey during September to November 1990, was compared with the period prevalence, gained from this observation study (Table 4.7). They are similar in ban 25 but significantly different in ban 15 ($p<0.001$). In the latter, the prevalence rate of bednet use from the census survey is about 15% higher than that from observation. The absentee rate is about twice as low in the survey as in the observation.

Table 4.7 Validity of bednet use.

Ban no.	Sleeping patterns	Observation data	(%)[1]	Census data	(%)[2]
15	Yes[3]	110	(72.8)	239	(87.5)
	No[4]	22	(14.6)	17	(6.3)
	Absent[5]	19	(12.6)	17	(6.3)
	Total (person-nights)	151	(100.0)	273	(100.0)
25	Yes[3]	47	(43.5)	47	(42.7)
	No[4]	50	(46.3)	53	(48.2)
	Absent[5]	11	(10.2)	10	(9.1)
	Total (person-nights)	108	(100.0)	110	(100.0)

1 - From 4 nights of observation on 11 households.
2 - From one day cross-sectional survey of the total households.
3 - Yes = sleeping under a bednet at least once during the night.
4 - No = never sleeping under a bednet throughout the night.
5 - Absent = never being seen in the household throughout the night.

4.4.2 Effects of untreated bednets on malaria incidence

Six pairs of bans were randomly allocated untreated bednets through the bednet fund programme during May 1990. Table 4.8 shows the comparisons of the malaria illness incidence rates between the untreated bednet intervention group and controls without additional bednets provided, before and after the intervention. The annual rate in each ban, before the intervention, was from the routine annual report of 1989. There were no details on age and sex structure of the population. The comparison between both groups was based on the crude rate in each ban. The routine data on 2 bans were recorded in the same name, therefore they represented only one unit of the intervention. This made the number of units among the control group to be 11, before the intervention (Table 4.8a). The 8-month incidence rate, during June 1990 to January 1991, was used for the comparison after the untreated bednet intervention in May 1990 (Table 4.8b). The census data were used to standardise the incidence rates by age and sex.

The average rate among the intervention bans was 0.78 times that amongst the controls in 1989 (Table 4.8a). This difference is not statistically significant. After the untreated bednet intervention, this rate difference became statistically significant ($p = 0.017$). The average rate among the intervention group was 0.56 (0.35 - 0.90) times that among the controls (Table 4.8b). This is equivalent to a 44% (10%-65%) effectiveness. However, the 22% difference before the intervention was high, though not statistically significant. Therefore, the unbiased estimate of the effectiveness may be only 28% (i.e. the reduction of rate ratio from 0.78 before to 0.56 after the untreated bednet intervention).

Table 4.8 Effects of bednet fund programme on a malaria incidence rate.

a) Before providing untreated bednets

	No additional bednets provided	Untreated bednets provided
Number of bans	11[1]	12
Number of persons/net[2]	2344/742 (3.2)	2217/854 (2.6)
Mean crude incidence[3] rate/ban	118.4	92.1
Rate ratio (95% confidence interval)[4]	1.00	0.78 # (0.44 - 1.38)

1 - Data on 2 bans were recorded under the same ban, therefore they represented only 1 unit.
2 - Data from the first census survey during January - March 1990.
3 - Incidence rate, as a no. of episodes/1,000 persons, were routinely reported during October 1988 to September 1989. There were no details on age and sex structure of the routine data for calculating a standardised rate in each ban.
4 - These were calculated on the natural logarithmic scale and converted back.
- No statistical significance

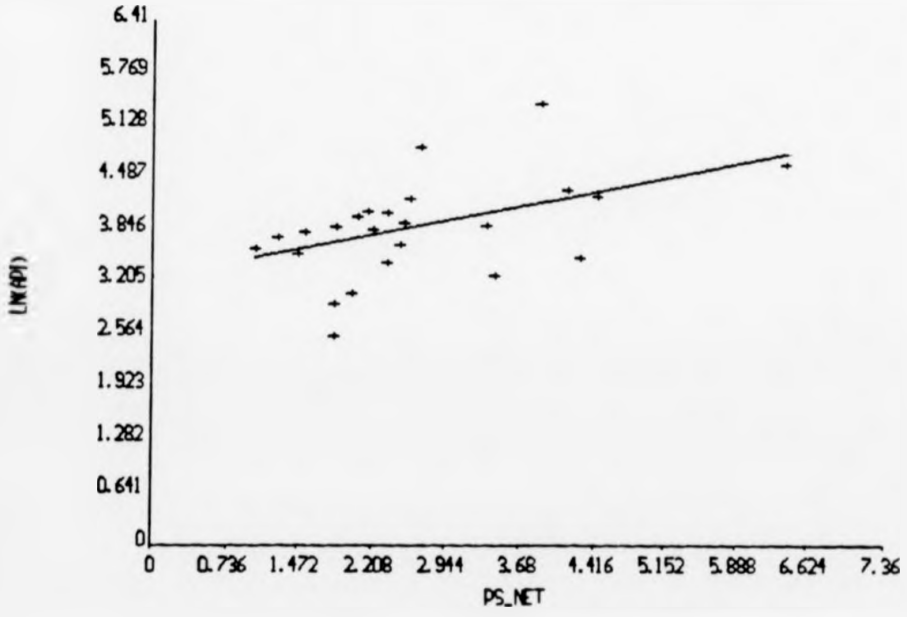
b) 8 months after providing untreated bednets through bednet fund mechanism in May'90

	No additional bednets provided	Untreated bednets provided
Number of bans	12	12
Number of persons/net[1]	2419/899 (2.7)	2292/1352 (1.7)
Mean standardised[2] incidence rate/ban (June'90 - Jan'91)	63.6	35.3
Rate ratio (95% confidence interval)[3]	1.00	0.56 ** (0.35 - 0.90)

1 - Data from the second census survey during September - November 1990.
2 - The standardised incidence rate during 8 month period, after the net distribution in May 1990. The demographic data, from the second census survey, were used for standardising the incidence rate by age and sex.
3 - These were calculated on the natural logarithmic scale and converted back.
** - p value = 0.017

Figure 4.8 shows the linear relationship between the average number of persons for each bednet in each ban and malaria incidence ($p < 0.05$; see Annex 2.7). These suggest that the differences in the incidence rates between the untreated bednet intervention and control groups can be attributed to the increasing number of untreated bednets in the intervention bans. This can also explain the difference observed before the intervention.

Figure 4.8 Relationship between incidence (log_API) and average number of persons/net.



4.4.3 Effects of the lambda-cyhalothrin impregnation programme

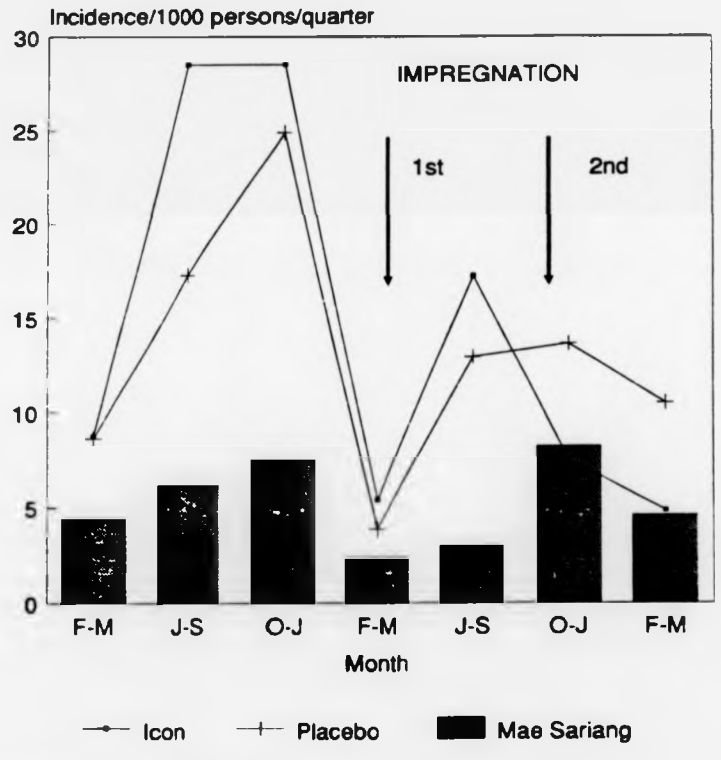
One ban in each of the 12 pairs was randomly allocated community-wide impregnation of villager bednets with either lambda-cyhalothrin or placebo. Table 4.9 shows that the randomisation resulted in 2 comparable groups. The age- and sex-adjusted incidence rates were equal to 58.6 episodes per 1,000 persons per year in both groups (the rate ratio is equal to 1.00). The numbers of persons per bednet, before the second distribution of untreated bednets in February 1991, were 2.1 in both groups. After the distribution, both numbers decreased equally to 1.8.

Table 4.9 Comparability of incidence rates between the lambda-cyhalothrin and placebo impregnation groups.

	Placebo impregnation	Lambda-cyhalothrin impregnation
Number of bans	12	12
Number of persons/net After 1st distribution[1] in May 1990	2889/1385 (2.1)	1822/866 (2.1)
After 2nd distribution[2] in February 1991	2858/1589 (1.8)	1852/1057 (1.8)
Mean standardised[3] incidence rate/ban (Feb'90-Jan'91)	58.62	58.56
Rate ratio (95% confidence interval)[4]	1.00	1.00 (0.62 - 1.51)

1 - Data from the second census survey during September - November 1990.
2 - Data from the third census survey during September - October 1991.
3 - Annual incidence rates (episodes/1,000 persons/ban) were standardised by age and sex, using the demographic data from the second census survey.
4 - These were calculated on the natural logarithmic scale and converted back (see Annex 2.8).

Figure 4.9 Incidence rate/quarter, by intervention.



February 1990 - May 1992.

4.4.3.1 Effects on malaria illness

Figure 4.9 shows the trend of malaria illness incidence, 12 months before and 16 months after the impregnation. The incidence in each quarter is plotted to reduce the variation of the monthly incidence due to a small number of cases in each month. This also establishes a clearer comparison of the trend over time. The incidence rates in both groups were also compared with the average incidence of the whole of Mae Sariang district. Before the impregnation, the crude incidence rates in the insecticide group were higher than those in the placebo group in every quarter. The rates in both groups were higher than the rate in the whole area. After the first impregnation during February to March 1991, the trends in both groups were decreasing and the rate in the insecticide group was still higher than the other. The second impregnation, previously planned to start in September 1991, was delayed to October due to the rains. After this impregnation during October to November 1991, the incidence rate in the insecticide group decreased to a level considerably lower than the rate in the placebo group and reached the rate in the whole area. The study ended in May and all bans resumed DDT spraying as before.

Table 4.10 compares the age- and sex-adjusted rates between both groups during 8 month periods after each impregnation. After the first impregnation, the adjusted 8-month rate in the insecticide group of 14.0 episodes/1,000 persons was slightly higher than the 11.6 episodes/1,000 persons in the placebo group, but this was not statistically significant. After the second impregnation, the rate in the insecticide group decreased to 8.3 while the other increased to 21.5 episodes/1,000 persons. This resulted in about 58% in the rate difference. The statistical variations were progressively increasing when the incidence rates were decreasing. These resulted in a wide confidence interval of the difference and the p value was 0.09. When all data after impregnation were pooled, the pooled rate ratio was 0.74. This was equivalent to 26% reduction, but not statistically significant (see also Annex 2.8).

Table 4.10 Effects of the lambda-cyhalothrin impregnation programme on the malaria incidence rate.

	Placebo impregnation	Lambda-cyhalothrin impregnation
Number of bans	12	12
After the first impregnation (Feb'-Sept'91)		
Overall household coverage (range in each ban)	58.4% (24.2 - 100.0)	76.2% (59.3 - 100.0)
Mean standardised[1] incidence rate/ban	11.64	14.00
Rate ratio[2] (95% confidence interval)[3]	1.00	1.19 (0.50 - 2.56)
After the second impregnation (Oct'91-May'92)		
Overall household coverage (range in each ban)	30.9% (8.1 - 100.0)	49.0% (33.9 - 92.9)
Mean standardised[1] incidence rate/ban	21.49	8.34
Rate ratio[2] (95% confidence interval)[3]	1.00	0.42 @ (0.16 - 1.05)
16 months summary (Feb'91-May'92)		
Rate ratio[2] (95% confidence interval)[3]	1.00	0.74 (0.52 - 1.07)

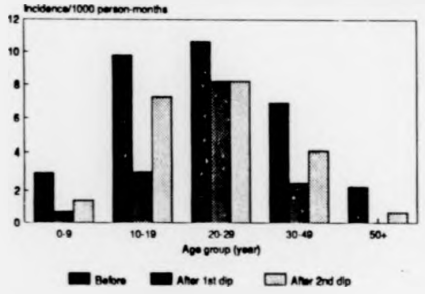
1 - Rates, during 8 month period (episodes/1,000 persons/ban), were standardised by age and sex, using the demographic data from the third census survey.

2 - Mean rate ratio on the logarithmic scale is slighly different from the rate ratio of true rate. The equivalent value on the log scale = $\log_e$(rate + 1) (see Annex 2.8).

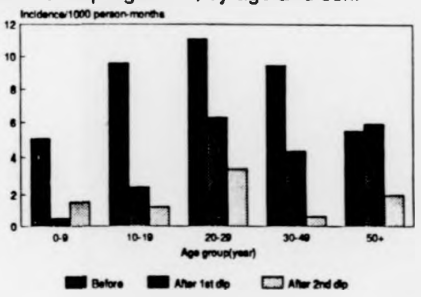
3 - These were calculated on the natural logarithmic scale and converted back.

@ - P value = 0.09 by paired t-test (< 0.05 by Wilcoxon signed-rank test, see Annex 2.8).

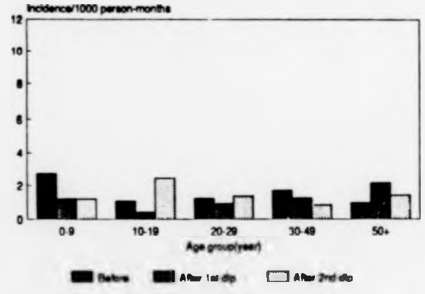
Figure 4.10 Crude rate trends before and after impregnation, by age and sex.



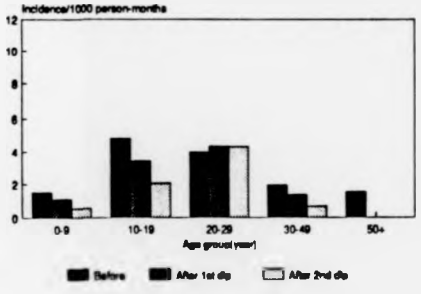
Males, Placebo-treated bednets



Males, Icon-treated bednets



Female, Placebo-treated bednets



Female, Icon-treated bednets

Figure 4.10 shows the crude rate trends, by age and sex, 12 months before and 8 months after the first and second impregnation in both the insecticide and placebo groups. A consistent decrease of the crude rate was observed amongst males 10-59 years of age. Analysis of the baseline data by age and sex revealed that the baseline average incidence rate in each age group and sex, in the same pair of ban, were not comparable between both groups (Table 4.11). The average rate ratios were considerably different from 1.00 except in male children of less than 15 years. Therefore the baseline data were included in the analysis on the effects of the insecticide impregnation (see Annex 2.8c). The difference of rate ratio from 1.00 reflects the effects of the impregnation. A significant difference was only found among adult males after the second impregnation. The rate ratio difference was equal to an 84.4% reduction of the incidence rate, taking into account the baseline data and the change of the rate in the placebo control matched ban (95% confidence interval, 0.04 - 0.62; $p < 0.02$). The other groups also showed consistent decreases, after the second impregnation, but these were not strong enough to overcome the statistical barrier.

Table 4.11 Incidence rate ratio (Icon^R/placebo), by age and sex.

Age (year)	Crude rate ratio Male	Female	Adjusted rate ratio[1] Male	Female
12 months before the intervention				
0 - 14	1.023	0.479	1.00	1.00
15+	0.543	1.775	1.00	1.00
8 months after the 1st impregnation				
0 - 14	0.877	1.287	0.857	2.688
15+	0.456	1.659	0.839	0.934
8 months after the 2nd impregnation				
0 - 14	0.589	0.544	0.575	1.136
15+	0.085	0.831	0.156**	0.468

1 - The rate ratios were adjusted by taking into account the prior rate ratio (see Annex 2.8c).
** - p value < 0.02

4.4.3.2 Effects on prevalence of infection

Mass blood surveys were done during October to November each year, before and after impregnation. Table 4.12 shows comparisons of the survey coverage and age- and sex-adjusted prevalence rates in both groups, before and after impregnation. Before the impregnation, the average adjusted prevalence rate in the insecticide group was 0.57%, lower than the rate of 2.26% in the placebo group. The rate ratio was 0.30 with a wide confidence interval ($p = 0.096$) due to the small number of positive slides in each ban. After the impregnation, the adjusted rate in the insecticide group decreased to 0.29%, significantly smaller than the rate in the placebo group, which also decreased to 1.57%. The rate ratio was 0.19 (95% confidence interval, 0.05-0.67; $p<0.02$). Although the rate difference before the impregnation was not statistically significant, the size of the difference was large and should be taken into account. The rate ratio adjusted for the prior difference was 0.64 (95% confidence interval, 0.09 - 4.44). The unbiased estimated effects of the impregnation on the prevalence of infection was 36% but this is not statistically significant ($p >0.50$).

Table 4.12 Effects of lambda-cyhalothrin impregnation on prevalence of infection.

	Placebo impregnation	Lambda-cyhalothrin impregnation
Number of bans	12	12
Before impregnation (Oct-Nov'90)		
Overall survey coverage[2] (range in each ban)	59.3% (37.8 - 89.5)	70.8% (50.0 - 94.9)
Mean standardised prevalence rate/ban	2.26%	0.57%
Rate ratio[3] (95% confidence interval)[4]	1.00	0.30# (0.07 - 1.28)
After impregnation (Oct-Nov'91)		
Overall survey coverage[2] (range in each ban)	62.2% (38.1 - 119.6)	83.2% (75.1 - 125.0)
Mean standardised prevalence rate/ban	1.57%	0.29%
Rate ratio[3] (95% confidence interval)[4]	1.00	0.19 @ (0.05 - 0.67)
Adjusted rate ratio[5] (95% confidence interval)[4]	1.00	0.64 (0.09 - 4.44)

1 - One pair of bans was excluded due to incompleteness of the first survey during Oct-Nov'90.
2 - See Annex 2.9d.
3 - Mean rate ratio on the logarithmic scale is slightly different from the rate ratio of true rate. The equivalent value on the log. scale = $\log_e$(rate + 1).
4 - These were calculated on the natural logarithmic scale, and converted back to a normal scale.
5 - The baseline values are taken into account for unbiased estimation of the impregnation effect (see Annex 2.9a).
- P value <0.10
@ - P value <0.02

Table 4.13 Prevalence rate ratio (Icon[R]/placebo), by age and sex.

Age (year)	Crude rate ratio Male	Female	Adjusted rate ratio[1] Male	Female
Oct-Nov'90 before the intervention				
0-14	0.201	0.503	1.00	1.00
15+	0.148	0.368	1.00	1.00
Oct-Nov'91 after the impregnation				
0-14	0.141	0.304	0.700	0.605
15+	0.296	0.535	2.000	1.455

1 - The rate ratios were adjusted by taking into account the prior rate ratio (see Annex 2.9b).

Table 4.13 shows the prevalence rate ratio (lambda-cyhalothrin/placebo) by age and sex, analysed in the same way as described in Table 4.11 on the age- and sex-specific incidence rate ratio. The rate ratios were considerably different from 1.00 before the impregnation. Therefore they were included in the analysis of the effects of the impregnation. The adjusted results showed no significant changes of the prevalence rate ratio after impregnation.

4.4.3.4 Dose related effects

Table 4.14 shows the effects of impregnation, with 3 aqueous dilution factors of 5% emulsified concentrate lambda-cyhalothrin solution, 100, 200 and 300, on malaria illness incidence and prevalence of infection. Before the impregnation, the rate ratios were considerably different from 1.00, suggesting unbalanced baseline rate ratios. They were included in the analysis of effects of different dosages of impregnation. There were no suggestive trends of dose-related effects. Analysis of variance revealed no significant difference of the means of either incidence or prevalence rate ratios among these 3 dosages.

Table 4.14 Dose-related effects.

a) On malaria incidence

	Average standardised-incidence rate ratio					
	Before adjustment			After adjustment		
Aqueous dilution factor of 5% EC Icon^{R}	1:100	1:200	1:300	1:100	1:200	1:300
Number of pairs	3	5	4	3	5	4
12 months before the impregnation	0.920	0.700	1.659	1.000	1.000	1.000
8 months after the 1st impregnation	0.338	1.586	2.121	0.368	2.718	1.284
8 months after the 2nd impregnation	0.178	0.690	0.416	0.189	1.221	0.174
16 months summary	0.397	0.782	0.946	0.513	1.221	0.472

1 - The rate ratios were adjusted by taking into account the prior incidence rate ratio (see Annex 2.10a).

b) On malaria prevalence

	Average standardised-prevalence rate ratio					
	Before adjustment			After adjustment		
Aqueous dilution factor of 5% EC Icon^{R}	1:100	1:200	1:300	1:100	1:200	1:300
Number of pairs	3	4	4	3	4	4
Oct-Nov'90 before the impregnation	0.718	0.047	1.000	1.000	1.000	1.000
Oct-Nov'91 after the impregnation	0.106	0.378	0.150	0.147	8.101	0.150

1 - The rate ratios were adjusted by taking into account the prior prevalence rate ratio (see Annex 2.10b).

4.4.4 Side-effects of the impregnation

There are 2 ways of being exposed to the insecticide; during the dipping process and after the treated bednets have been dried.

4.4.4.1 During dipping of bednets

Two out of seven workers who took part in dipping villagers' nets suffered from sneezing and running nose. One worker helped villagers dry their nets and scratched her right eye without washing her hand. She immediately suffered conjunctivitis in her right eye, which was cured after 3 days of steroid eyedrop medication. All these effects happened with the 1:100 aqueous solution.

4.4.4.2 When using the treated bednets.

Surveys were carried out a week after the first dipping in each ban. A total of 279 households were randomly selected. About 70% brought their nets for impregnation. Only 34% of households used the treated nets within one week of the impregnation. Results are shown in Table 4.15. Household members suffered significantly more from the lambda-cyhalothrin treated nets (56%) than from the placebo ones (23%) (p value = 0.01). The 1:100 dosage significantly gave a higher rate of side-effects than the others (p value = 0.03). Sneezing was the most common side-effect (about 90%). Other side-effects were mild swelling of the face, dizziness and headache. All these side-effects disappeared after several days. This period depended on the concentration of the insecticide solution, in which the bednets were dipped.

Table 4.15 Results of side-effect surveys a week after the first impregnation.

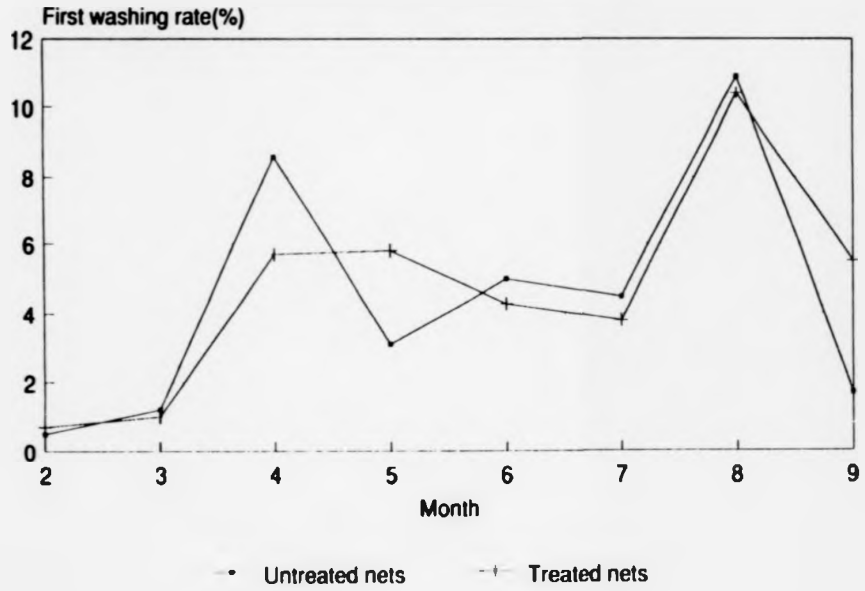
Treatment	Aqueous dilution factor	Households experiencing any discomforts			Total[1]
		Sneezing (%)	Others (%)	None (%)	
5% EC lambda-cyhalothrin	1:100	12 (80)	-	3 (20)	15
	1:200	2 (17)	2 (17)	8 (67)	12
	1:300	3 (43)	-	4 (57)	7
	Total	17 (50)	2 (6)	15 (44)	34
Placebo	1:100	3 (25)	1 (8)	8 (67)	12
	1:200	1 (17)	-	5 (83)	6
	1:300	-	2 (15)	11 (85)	13
	Total	4 (13)	3 (10)	24 (77)	31

1 - A household was used as a unit of analysis. Only about one third of the households with treated bednets used them during the first week after the first impregnation.

4.4.5 Washing of treated bednets

Questions on washing frequencies and time were added to the third census survey during October to November 1991. Although questions were asked about any washings since January 1991, the analysis focused only on washings during February to September 1991. Among a total of 2,636 bednets, 60% of them were not washed, 26% were washed once and 14% more than once. Figure 4.11 shows rates of the first wash in each month by treatment. The patterns in both groups were similar. There were 2 peaks of the first wash, the smaller in April and greater in August. However, the crude washing rate of 36% among the insecticide treated bednets was significantly lower than the rate of 43% among the placebo treated bednets ($p<0.001$). This suggested that villagers were aware of the benefits of the insecticide treated bednets and trying to keep them unwashed.

Figure 4.11 First washing rates after impregnation, by treatment.



Mae Sariang, Thailand, Feb-Sept'91

Table 4.16 Dose-related washing after the insecticide impregnation.

a) Bednets treated with lambda-cyhalothrin

Washed	No. of bednets in bans receiving the same dosage							
	1:100		1:200		1:300		Total	
	Treated		Treated		Treated		Treated	
	Yes	No	Yes	No	Yes	No	Yes	No
Yes	67	6	113	30	60	29	240	65
No	129	46	129	81	168	55	426	182
Total (unk.)	195	52	242	111	228	84	666	247
	(2)		(123)		(19)		(144)	
% washed	34.2	11.5	46.7	27.0	26.3	34.5	36.0	26.3
Relative washing rate$_{tr/untr}$ (95% ci.)	2.97**	1.00	1.73**	1.00	0.76	1.00	1.42#	1.00
	(1.37-6.48)		(1.16-2.28)		(0.59-1.23)		(1.12 - 1.80)	

b) Bednets treated with placebo

Washed	No. of bednets in bans receiving the same dosage							
	1:100		1:200		1:300		Total	
	Treated		Treated		Treated		Treated	
	Yes	No	Yes	No	Yes	No	Yes	No
Yes	121	166	23	19	137	36	281	221
No	84	56	52	56	244	122	380	234
Total (unk.)	205	222	75	75	381	158	661	455
	(345)		(75)		(43)		(463)	
% washed	59.0	74.8	30.7	25.3	36.0	22.8	42.5	48.6
Relative washing rate$_{tr/untr}$ (95% ci.)	0.79**	1.00	1.21	1.00	1.58**	1.00	1.02	1.00
	(0.69-0.91)		(0.66-1.90)		(1.24-2.38)		(0.89 - 1.16)	

- Summary relative risk by Mantel-Haenszel Weighted method, p value<0.01
** - p value < 0.005

From the side-effect survey, many bednets treated with a 1:100 dosage were washed due to their strong side-effects. To study the possible dose-related washing, the rate of washing was compared between bednets treated with different dosages and untreated bednets in the same ban (Table 4.16). Among bednets receiving insecticide impregnation (Table 4.16a), the rate of being washed was 2.97, 1.73 and 0.76 times the rate among untreated bednets in the same ban (p value = 0.002, 0.003 and 0.394 respectively). A summary of these relative rates was 1.42, strongly suggesting that a treated bednet carried a higher chance of being washed than an untreated bednet under the same social situation ($p < 0.01$). The higher the dosage the greater the chance of a treated bednet being washed. This is likely to be caused by the side-effects of the insecticide treated bednet.

Among bednets treated with placebo (Table 4.16b), there was a reverse relationship found in the insecticide group. However, the summary relative rate of washing was 1.02 and not statistically significant ($p = 0.87$). There were complaints about fungi growing on a placebo-treated net. The placebo solution was made from a white water colour with the addition of preservative powder (sodium benzoate). This might encourage a villager to wash a placebo treated net.

In one ban receiving 1:100 dosage of the lambda-cyhalothrin impregnation, a water-soluble ink was marked on the treated bednets after they had been dried. Fifty percents of households were randomly selected for a survey of the persistence of the ink mark 7 months after the first impregnation. A total of 33 treated bednets were examined and the ink marks were found on only 10 of them, with 3 bednets having faint ink marks (Table 4.17). This gave about a 70% washing rate, which was significantly greater than the same rate estimated from the census survey data ($p<0.002$). This suggests that the actual washing rate in general could be higher than villagers reported. The size of the difference may depend on socio-cultural conditions in each community.

Table 4.17 Validity of washing rates from the census survey in Ban no.15.

	Census survey Total	washed (%)	Ink-mark survey Total	absent (%)	faint (%)
Untreated nets	39	2 (5.1)	19	n.a.[1]	n.a[1]
Treated nets	115	43 (37.4)	33	23 (69.7)	3 (9.1)

4.5 Discussions

4.5.1 General epidemiological and socio-cultural conditions

4.5.1.1 Epidemiology of malaria morbidity and infection

The overall annual incidence of 56.68 episodes/1,000 persons was similar to the level of morbidity reported from Hainan province, China (Li Zuzi et al in: Curtis et al, 1990), in which a similar case detection system was used. The high proportion of P.falciparum cases (90%) was similar to those in most forest-related areas in Southeast Asia (Sharma and Kondrashin, 1991). The prevalence of infection was lower than 2%. The age- and sex-specific incidence and prevalence had different patterns. Young adult males of 20 - 39 years of age had the highest incidence rate but a prevalence rate of infection similar to other groups. This can be explained by the age- and sex specific patterns of movements (see the previous chapter on population movements in the area). The coverage of the mass blood survey was moderate. Adult males had lowest coverage rate (Table 4.3). This could be due to a high movement rate among this group as shown in chapter 3. This suggested that frequent movers were likely to be missed. The similar low prevalence rate among different age and sex groups suggested that the risk of malaria infection within the village did not depend on age and sex and the high malaria incidence rate among adult males was directly related to movements.

4.5.1.2 Socio-cultural conditions

DDT spraying had long been implemented in the area. This inevitably made villagers familiar with the knowledge of malaria disease and transmission. Although only 25% of them experienced malaria illness, more than 80%

knew that the disease could cause death and about 58% knew that the disease is transmitted by mosquitoes (see 1.3.3.a). Moreover, the Karen words for malaria are 'pa tso tsei' which means 'mosquito-toxin fever'. These might have encouraged them to go to hospitals or malaria clinics for blood examination when they became ill and suspected it to be malaria. This resulted in about 79% of cases being detected by hospitals and malaria clinics (see 1.2.1). Among the villagers who experienced a malaria illness before the study, 25%, 26%, 26% and 17% believed that they got the infection from within the village, farm or stream, forest in the area and forest in Myanmar border, respectively. These beliefs could be the reasons for the high rates of bednet being taken during agricultural (73%) and forest (88%) moving (see the chapter on population movements).

More than 90% of villagers used to sleep under a bednet. Most of them (75%) firstly experienced this during adult life, suggesting that bednets only recently became available to them. About 85% perceived and used a bednet for preventing mosquito nuisance rather than malaria illness (see 1.3.3.b). The reasons for not using a bednet were hot weather, no bednets available and an unfamiliarity with a bednet in old age people. The study on the prevalence of bednet usage, by both observation and close-ended questionnaires, confirmed that the use of bednets increased when the availability of bednets increased. The bednet fund mechanism was used to ensure that villagers had perceived the cost implication of sleeping under a bednet. Therefore, if they bought new bednets, they should intend to use them for various purposes; regular use within the household or farm huts, keeping them in reserve or for guests' use and carrying them when moving. There was no cultural belief against using bednets. The main reason was a financial constraint. The bednet fund, once formed, may alleviate this problem to a certain level depending on the amount of money raised and the socio-economic conditions of villagers. However, the self sustainability of the fund also depended on the strength of the community organisation.

4.5.2 Design for measuring effectiveness of the trial

4.5.2.1 Choice of design

This study was designed to avoid flaws found in many trials (WHO, 1989; Bermejo & Veeken, 1992). Randomised controlled trials are the standard way of evaluating new therapeutic agents and procedures at the individual level (Kirkwood and Morrow, 1989). Randomisation would assure that confounding factors are distributed equally into each comparison group. The difference of the outcome measure among the intervention group from that in the control would be directly attributed to the intervention. Extending this method to evaluate the effects of the impregnation programme, using a community as a unit of intervention, presented many difficulties. It is extremely difficult and expensive to include enough communities to have a strong statistical power of detection of difference. Moreover, to cope with natural year to year variation, the complete design should include baseline pre-intervention data so that the yearly change of an outcome measure in the intervention group can be compared with that in the control group (Molineaux, 1991). Therefore the difference between the net change among the intervention group and the control could be attributed to the intervention with the least bias. Matching of the study communities on important confounding factors would increase the statistical power (Smith and Morrow, 1991).

The routine data collected by the malaria control programme in Thailand were of reasonable quality. Although, the quality was not good enough to be pre-intervention baseline data, because there were no age and sex demographic details, they were very useful for sampling. The study was designed in a step-wedge style, commencing with an untreated bednet fund programme in the first year and followed by impregnation in the second year. The main aim was to measure the effectiveness of the impregnation programme. However, the effectiveness of untreated bednets was also a matter of interest for the control point of view. This design allowed the latter to be assessed, though not precisely. This however paid the price of decreasing statistical power of the effectiveness of impregnation in the later period (Kirkwood and Morrow, 1989).

4.5.2.2 Choice of outcome measures

Malaria fever, clinical malaria or malaria deaths are recommended as appropriate outcome measures for trials (WHO, 1989). These are more sensitive to control measures than parasitaemia alone (Snow et al, 1988c; WHO, 1989; Alonso et al, 1991; Bermejo & Veeken, 1992). In Thailand the malaria death rate is low and attempts to measure the effects of the control measure on malaria mortality are expensive. Malaria fever and clinical malaria are under the surveillance system, comprising the passive and active case detection systems. Every malaria case has been confirmed by parasitaemia. The case detection systems have been operating since the implementation of the malaria eradication campaign. The perception and awareness of villagers are high and malaria cases are detected early. These patterns may be comparable to many countries in the region which have similar malaria control histories. The annual incidence of malaria illness is called an annual parasite incidence (API) and has been central in evaluating the malaria situation and planning for control of the disease in this region (Sharma and Kondrashin, 1991). Thus, the selection of this measure was relevant to the control practices in the region and the results should enable some degree of generalisation to other similar areas in the region.

However, the prevalence of parasitaemia was also measured as a minor outcome. This allowed the results of this study to be comparable to others, based on measuring the parasitaemia rate. The low prevalence of parasitaemia in this area would also have made the trial very expensive if this measure was carried out sequentially as a major outcome in assessing the effectiveness of impregnation. Thus, the mass blood surveys were carried out only once during the middle of the transmission season in each year.

4.5.2.3 Sampling

The calculation of sample size was based on pre-study routine data. A total of 20 bans was needed to assure statistical power. However, after the introduction of the bednet fund programme, the incidence rate was expected to decrease before impregnation. This would increase the statistical variation and reduce statistical power for the evaluation of the impregnation programme in the second year. Thus, the total samples were raised to 24 bans at the beginning of the study, to

compensate for this reduction. They were also matched by factors considered to be important confounding factors. All bans eligible for the inclusion criteria were surveyed and matched. The best 24 matched pairs were included in the study.

4.5.2.4 Matching

It was difficult to get a pair of communities which have similar patterns of important confounding factors. The matching on a geographical characteristic had to be made by eye, to collect various ecological indicators in each community for this purpose was too expensive. The large year to year variation of malaria incidence could make matching by API invalid the year after. However, with randomisation, hopefully the variation would be equal in both groups. The ethnic group was reported as another important factor related to malaria (Greenwood et al. 1987). This was easily matched. It may be assumed that matching by the ethnic group would result in a pair with similar behavioral risk factors such as movements and bednet usage. Analysis of the statistical variations found that they were slightly greater with an unmatched analysis than a matched-pair analysis, suggesting that matching in this study improved the statistical validity.

4.5.2.5 Placebo controlling

This was deliberately done to blind both villagers and malaria workers on the type of intervention. The aim was to reduce the possible biases introduced into the results. The response of villagers to the side-effect survey could be affected by this knowledge. The case detection efforts may not be the same in both groups if the malaria workers have a selective intention on either the insecticide or placebo group. There was some recognition by the villagers and malaria workers between both impregnations due to the difference in side-effects during and shortly after the impregnation; and the effectiveness of the insecticide treated bednets in preventing insect nuisances, exposed the placebo treated nets. However, the side-effect survey a week after the first impregnation revealed apparent side-effects in the placebo group demonstrating that many people were unaware of the difference.

4.5.2.6 Data analysis

Because the sampling scheme was based on a natural logarithmic value of the incidence rates, the data had to be analysed in the same way. The small number of bans in each group produced a wide statistical error, but logarithmic transformation reduced this variation. Matching also reduced the wide variation to a certain level. Therefore, pair analyses of the natural logarithmic value were carried out with the incidence and prevalence rates. On the logarithmic scale, a rate ratio was equivalent to a rate difference on the normal scale. For example , a pair of bans with the same rate will have a rate ratio of 1 and a rate difference of 0. When the rate ratio is transformed to a logarithmic scale, the transformed value of 1 is also equal to 0. Thus, the transformed rate ratios are equivalent to the rate differences on a normal scale but are more stable and have narrower statistical variations. However, when the absolute values of those rates come down to 0, the rate ratios give wide variations. The variation also depends on the total population in each ban, if it is small, the rate will also have a wide variation following a change of only one case. To cope with these problems, the population in each community should be large enough. However, most large communities had a good socio-economic condition and low malaria morbidity. To include enough pairs of these large communities for evaluating the effectiveness of the trial would be too expensive and considered not to be a cost-effective way. Hence, this study was an attempt at compromise. Bans with a population lower than 50 were avoided and included only when they were well matched with each other in all criteria mentioned.

The incidence rates were also standardised by age and sex before being transformed. The overall population of the 24 bans was used as a standard population. This was done to avoid a bias leading to false conclusion when comparing age- and sex-dependent rates in 2 populations with different age and sex structures (Armitage and Berry, 1987).

4.5.3 Effects of the bednet fund programme

4.5.3.1 Pair-randomisation before the study

Table 2.8a shows that before the study, the mean crude incidence rate per ban was already higher amongst the control bans than the bans receiving bednet fund programmes. This might be because the number of randomised

pairs was small (only 12 pairs). Simple random sampling, with a small number of bans, could result in an imbalance of the outcome measure. Moreover, the pair-randomisation could double the imbalance. Although this imbalance was not statistically significant, the size of a 22% difference (mean rate ratio = 0.78) was considered to be too high and should be taken into account during interpretation of the difference, after the intervention of the bednet fund programme.

4.5.3.2 Effects on malaria incidence

After introduction of the bednet fund programme into half of the 12 pairs, the means of the standardised incidence rates per ban decreased in both groups. These could be due to the increase of untreated bednets in both groups; 21% in the control and 58% in the intervention group. However, the mean standardised rate among the intervention bans was significantly less than that in the controls and a mean rate ratio of 0.56 resulted in a 44% reduction (10% - 65%, $p<0.02$). The ratio is about 72% of the baseline mean rate ratio. Therefore, the unbiased estimate of the rate reduction, attributable to the bednet fund programme, could be about 28% after 8 months of the intervention. This estimate would be greater if the rates among bans receiving bednet fund programmes were compared with those among bans with no or few bednets. This effect was also confirmed by correlation analysis of the number of persons for a bednet and the incidence rate (on the natural logarithmic scale) in each ban (Figure 4.8 and Annex 2.7). The $\log_e$(incidence rate + 1) was increasing significantly when the number of persons/bednet increased ($r = 0.48$, $p<0.05$). In The Gambia, Snow et al (1988a) found about 37% effectiveness, when comparing the malaria morbidity among children receiving untreated bednets with the control group not receiving them. Although this was not statistically significant, the size of the effect was considered to be high. In China, Liu et al (quoted by Lu, 1991) reported the reduction of annual incidence rate from 180.8/1,000 to 0.45/1,000, 5 years after motivating the villagers to sleep indoors under bednets and giving them mass drug administration. However, the evaluations used different methodologies and could not be directly compared.

In summary, it can be confidently concluded that the bednet fund programme had increased the availability of untreated bednets in the intervention bans, this led to a significant increase in the bednet usage and resulted in about a 28% reduction of the malaria incidence after 8 months of the intervention.

4.5.4 Effects of the insecticide impregnation programme

4.5.4.1 Effects on the incidence rate

i) Trend of the effects

The trends of the crude incidence rate in figure 4.9 can lead to two obvious interpretations. The first is that the crude incidence rates among the study bans were higher than that of the whole district. The second is that lambda-cyhalothrin impregnation was more effective than the placebo impregnation in reducing the incidence rate but this was a slow effect, which could be only seen after the second impregnation. The reduction of incidence in both groups, after the impregnations, may be partly explained by the increasing number of bednets in both groups (Table 4.9). It may also be explained by a decreasing incidence in the whole district.

ii) Size of the effect

Table 4.9 shows that the random allocation of either the lambda-cyhalothrin or placebo impregnations to each ban in a pair, resulted in two comparable groups. The average number of persons/bednet and standardised incidence rate/ban were almost identical. The average standardised rate ratio was equal to 1.00. This ensures that the difference of the rate ratio from 1.00, i.e. the difference of the $\log_e$(rate ratio) from 0, after impregnations can be directly attributed to the difference of the impregnations. Because Figure 4.9 clearly shows that the trends after the first impregnation were considerably different from those after the second impregnation, the data were analysed separately after each impregnation. The results confirmed the trends observed. There was no significant difference between the average standardised rate in both groups although the average rate among the insecticide group was slightly higher than that among the placebo group (Table 4.10). After the second impregnation, the average rate among the insecticide group was about 2.4 times lower than that of the placebo group. The average rate ratio was 0.42. This is equivalent to a 58% reduction. However, when the incidence rate in each ban decreased to a

very low level, the statistical variation was increasing considerably (see Annex 2.8a). The p value by a paired t-test analysis was 0.09. When the data were pooled over the total 16 months after the impregnation, the average rate ratio was 0.74 (95% confidence interval, 0.50 - 1.11, $p < 0.15$). This is equivalent to a 26% reduction. Although this is not strong enough to give statistical significance, the trends of the effects is clear. It may be concluded that the lambda-cyhalothrin impregnation slowly added, on top of the untreated bednet programme, a 26% reduction of malaria incidence after 16 months of the impregnation. In China, most treated bednet trials resulted in at least a 50% effectiveness (Lu, 1991). However, the sizes and methodologies of the trials were not comparable with this study.

iii) Analysis by age and sex

Snow et al (1988c), using a similar methodology, reported a protective effects of 63% against malaria morbidity among Gambian children. Graves et al (1987) also found a reduction of malaria morbidity in under-5-year-old children. These effects were not found here. These could be due to the low level of morbidity among children in this area compared with those in The Gambia and Papua New Guinea. The effects were expected to be observed more in children and females, who showed high rate of bednet use in the village. In contrast, adult males were the ones who benefited most from the impregnation programme. The 84% effectiveness after the second impregnation was statistically significant at p value less than 0.02. This could be because they had the highest incidence rate, its reduction was therefore easy to detect. However, Kamol-Ratanakul and Prasittisuk (1992) also found a 66% protective effect of permethrin-treated bednets among migrant workers in the Eastern Thailand. This suggests that the mechanism of protection amongst adult males in this area might not be similar to that amongst children in other studies.

4.5.4.2 Effects on prevalence of parasitaemia

Although there was some 36% effectiveness of the lambda-cyhalothrin impregnation against the prevalence of parasitaemia, this was not strong enough to give statistical significance. The age- and sex-adjusted rate ratio showed reductions among children and an increase among adults. None of these were

statistically significant. A very small parasitaemia resulted in a very wide statistical variation and it is difficult to draw any conclusions from the results. However, because the prevalence of parasitaemia reflected the situation closer to the transmission within the village than did the incidence of malaria illness, it may be concluded that the impregnation programme seemed to have no significant protective effect against malaria infection within the village in this area. This might be due to the low coverage of the impregnation. The small number of study pairs prevented further useful analysis.

These findings suggested that the insecticide impregnation programme gave better protection against malaria illness incidence than the parasitaemia. These were similar to the results from The Gambia (Snow et al. 1988c). However, because the local epidemiological, ecological and socio-cultural conditions were likely to be quite different, the mechanisms of the effect were likely to be different.

4.5.5 Mechanism of the effects

When comparing the sleeping patterns (Figure 4.4) and the biting patterns (Annex 2.11) of the potential vectors, it is clear that an untreated bednet could not totally protect a villager all night. There was a chance of being bitten during the dusk and dawn. The bednet fund programme considerably increased bednet use rate, resulting in an increased proportion of villagers protected by untreated bednets which could be a reason for the reduction in the incidence of malaria illness. It was not clear whether this was mainly due to the reduction of man-vector contact within the residence or during moving. A more extensive study on the effects of untreated bednets on malaria illness during staying in the residence and moving could test this hypothesis.

After the insecticide impregnation, there were no significant effects on the prevalence of parasitaemia. This was likely to reflect the effects of the impregnation on malaria within the village. The significant reduction of the incidence of malaria illness among adult males, attributable to the lambda-cyhalothrin impregnation, suggested that the major protective effects might not take place in the village. The studies on the prevalence of bednet use and sleeping pattern in the village clearly showed that young adult males were the poorest bednet users. The study on villager movements also pointed out that they had the highest moving rate

and movements had been shown to be an important risk factor. The forest movement, of which more than 95% involved adult males, carried the highest risk of malaria illness. The studies of villager knowledge about the place of infection showed that most of them were aware of this risk (see 1.3.3.a) and 88% of the forest movers took a bednet with them during moving. After the impregnation, the insecticide treated bednets would give better protective effects than the placebo treated nets, being taken during moving. These effects could be slow due to the average moving rate being only 11%. During the beginning of the dry season, the forest moving rate was increasing. This might have resulted in more protective effects against malaria illness during the dry season, as shown in the results.

Other factors needing to be considered were the coverage of the insecticide impregnation, the dosage, the washing rate of treated bednets, the timing and interval of the impregnation. The coverage rate of impregnation seemed not directly related to the effectiveness of the programme. The first had higher household coverage than the second impregnation but showed less effects. The different dosages of the insecticide solution did not lead to a dose-response effect on either the incidence of malaria illness or the prevalence of parasitaemia. In contrast, the highest dosage caused the highest rate of side-effects. The side-effects found were similar to those reported elsewhere (Njunwa et al, 1991; Baskaran et al, 1991; Moretto, 1991; Chester et al, 1992). These might have discouraged villagers to bring their bednets for the second impregnation.

The washing rates were available only after the first impregnation. Nevertheless, the rate of 40% was high, considering that this was an underestimated rate compared with the washable ink-mark study. The findings also showed that these were dose-related responses. The higher the dose of insecticide solution the more treated bednets were washed. only a dosage of 1:300 gave good compliance. The target dosage of 10 mg/m^2 was aimed at but the actual dosages were lower than the target dosages (see Annex 2.4). These were also observed in other reports (Miller et al, 1991; Lindsay et al, 1991). However, bioassay tests on the treated bednets, used by villagers in the pilot area, gave at least a 6-7 month period of killing effects. Therefore, this dosage was used in all bans in the second impregnation.

The trend of bednet washing in this area also caused concern. The first peak of washing in April was a cultural event during the traditional new year in April. The second peak in August might be due to the availability of water during late rainy season. This suggested that the insecticide could have been washed out to some extent before the second impregnation in October. The right timing should be after April and August.

The low coverage and high washing rates would considerably reduce the effects of insecticide impregnation. Despite these weaknesses, adult males still benefited from the impregnation. These led to a suggestion that the beneficial effects were taking place outside the village during moving. Therefore, it may be more cost-effective if the priority of the impregnation is given to bednets that were normally used during moving. However, these were indirect findings and direct studies on the protective effects of treated bednets against malaria illness, acquired from circular movements, are needed.

4.5.6 Prospects for the bednet fund and impregnation programme

The situation in this area was closer to the Chinese than the African. Although the Chinese studies might have contained methodological flaws (Bermejo & Veekan, 1992), the consistency of the results suggested that their success was real; however, the size of the effect may be interpreted with caution. Whether their successes could be repeated elsewhere remains to be seen.

In this study, the evidence of effectiveness of the bednet fund programme (net distribution) was stronger than that of the impregnation programme. The latter showed a slow trend of the overall effects. However, the effects were significant and strong among the high risk adult males, despite many weaknesses of the impregnation operation. This was encouraging and possibly resulted from the protection of adult males during moving. If the impregnation is expanded to cover the whole area, the effects could be better. Washing habits should be considered for planning the timing and interval of impregnation. Villagers should possess enough bednets to use both within the residence and during moving. The full benefits of the impregnation programme could be achieved if villagers are involved in the dipping process.

It was clear that Karen people in this area were accustomed to sleeping under bednets and showed a commitment to buying them for their own use. The bednet fund programme could be a starting point for encouraging further community involvement in malaria control. When the fund is strong, the expenses of impregnation may be incorporated gradually. This can take a period of time before it is achieved and the malaria control programme needs to take responsibility for impregnation. However, an impregnation programme alone may only reduce malaria morbidity to a certain level. The early evening and early morning biting habits of the vectors are not prevented by treated bednets in this area. Other personal protection measures are also need to be applied during these times. The expenses may also be incorporated into the well developed bednet fund.

4.5.7 Future research

Direct studies on a protective effect of untreated and treated bednets during various types of circular movement are needed to test the hypothesis raised above. The results can be used for setting priorities for the impregnation. An evaluation on performance of the bednet fund programme would also be useful for developing a better way of strengthening malaria control through community involvement. New insecticides with less side-effects and more washed-fastness need to be developed and evaluated in the field.

4.6. Conclusions

4.6.1 Adult males had the highest malaria incidence rate but the prevalence rates of malaria parasitaemia were similar in all age and sex groups.

4.6.2 Karens in this area had no cultural barriers against bednets. The bednet fund programme increased the availability of untreated bednets to them, resulting in an increase in the use of bednets and decrease in malaria morbidity.

4.6.3 The additional lambda-cyhalothrin impregnation programme gave a small and slow effect against malaria morbidity and no significant effect against the prevalence of parasitaemia. These might be due to a high washing rate after impregnation.

4.6.4 There were two peaks of washing in April and August. The target dose of 10 mg/m^2 (aqueous solution of 1:300 dosage of 5% EC lambda-cyhalothrin) gave good compliance and maintained killing effects for at least 6-7 months after impregnation. The proper timing for impregnation should be after April and August.

4.6.5 There were no dose-response effects of the impregnation on malaria morbidity but the highest dosage gave the highest side-effect rates. Moreover, the higher the dose, the more treated bednets were washed. Sneezing was the most common side-effects amongst users and disappeared after several days.

4.6.6 Despite a low rate of bednet use in the village, adult males benefited most from the impregnation programme. This might be due to the protective effect of treated bednets during moving and needs to be confirmed by direct studies.

Chapter 5
Conclusions and Recommendations

The conclusions from all results are summarised below. A list of recommendations on the malaria control and further research is also made.

5.1 Conclusions from the movement study

5.1.1 Short term movements during the transmission season were common. About 74% of villagers moved at least once. On average, villagers spent about 11% of their nights outside the residence during the season.

5.1.2 The first and second common reasons were for agricultural (farming, harvesting and looking after cattle) and forest activities (logging, reforestation works and forest patrolling) respectively. A small number of several hour movements for hunting and fishing during the night were also detected and expected to be largely underestimated. Adult males predominated in all types of movements.

5.1.3 The malaria incidence was directly related to the number and duration of movement. The risk of malaria illness during moving can be at least 7.8 times higher than staying in residence. Forest activity carried the highest risk, followed by agricultural and other activities respectively.

5.1.4 In general, about 60% of movers took a bed net with them. They tended to do so when they entered the forest (88%) or went to the farm (73%), slept under the temporary (87%) or semi-permanent shelters (75%), or when the moving duration was long (median = 8 nights). Very few of them took a bed net when they went to visit their relatives.

5.1.5 Untreated bed nets taken during moving might have given about 27% effectiveness but this was not statistically significant.

5.1.6 Analysis on the seasonality of malaria illness in relation to rainfall, vector density and movement, suggests the importance of agricultural activity and movements during the dusk and dawn.

5.1.7 The more extensive studies covering the whole year may elaborate more details about the possible role of movement in maintaining the infective reservoir in the forest.

5.2 Conclusions from the impregnation trial

5.2.1 Adult males had the highest malaria incidence rate but the prevalence rates of malaria parasitaemia were similar in all age and sex groups.

5.2.2 Karens in this area had no cultural barriers against bednets. The bednet fund programme increased the availability of untreated bednets to them, resulting in an increase in the use of bednets and decrease in malaria morbidity.

5.2.3 The additional lambda-cyhalothrin impregnation programme gave a small and slow effect against malaria morbidity and no significant effect against the prevalence of parasitaemia. These might be due to a high washing rate after impregnation.

5.2.4 There were two peaks of washing in April and August. The target dose of 10 mg/m^2 (aqueous solution of 1:300 dosage of 5% EC lambda-cyhalothrin) gave good compliance and maintained killing effects for at least 6-7 months after impregnation. The proper timing for impregnation should be after April and August.

5.2.5 There were no dose-response effects of the impregnation on malaria morbidity but the highest dosage gave the highest side-effect rates. Moreover, the higher the dose, the more treated bednets were washed. Sneezing was the most common side-effect amongst users and disappeared after several days.

5.2.6 Despite a low rate of bednet use in the village, adult males benefited most from the impregnation programme. This might be due to the protective effect of treated bednets during moving and it needs to be confirmed by direct studies.

5.3 Recommendations for malaria control

5.3.1 Risk of malaria illness caused by various types of movements should be integrated into health education processes. People should be encouraged to take a bednet with them, especially the pyrethroid-treated net.

5.3.2 The impregnation programme should be gradually expanded. All bans in endemic areas, especially with difficult accessibility, should be given priority. More attention should be put on the activities of villagers outside the village and the availability of a treated bednet during moving.

5.3.3 Bednet funds should be expanded to cover all bans in the endemic areas. The strong funds should be encouraged to take more part in the impregnation programme and other individual protection methods, such as selling repellents and mosquito coils.

5.3.4 Repellents should be promoted, especially during the dusk and dawn. The costs may be incorporated in a strong bednet fund programme.

5.4 Recommendations for further studies

5.4.1 A randomised control trial should be done to measure the effects of a treated bednet during moving on an individual basis. This should cover the whole year and efforts should be put in to measure movements during the dusk and dawn.

5.4.2 More impregnation trials, on a village basis, should be done to confirm the finding in this area and compare the effects of the treated bednets with DDT spraying on malaria morbidity. The good surveillance system should be used as a major source of morbidity data due to its sensitivity. Villager movements should also be measured during the studies.

5.4.3 Evaluation of the bednet fund performance should be done to find a better way to encourage more community involvement in malaria control.

5.4.4 Economic evaluation of the bednet fund and impregnation programme should give better chances for proper priority setting and decision making.

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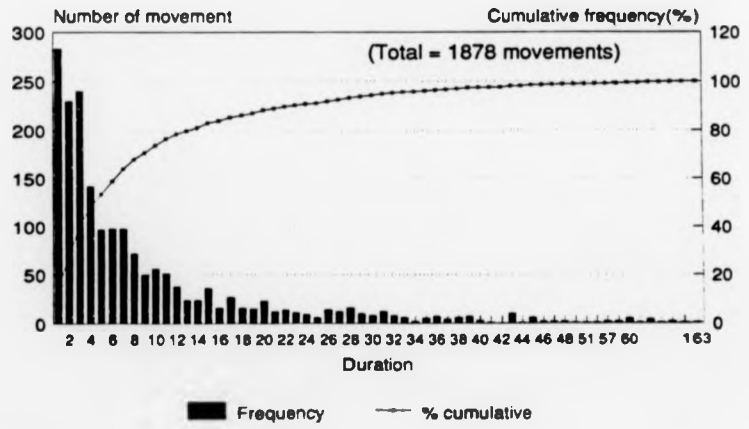
ANNEX 1

DETAILS ON THE MOVEMENT STUDY

Annex 1.1 Proportions of samples included, by age and sex.

Age (yr)	Sex						Total		
	Male			Female					
	Total	Sample	(%)	Total	Sample	(%)	Total	Sample	(%)
0-14	242	96	39.7	223	84	37.7	465	180	38.7
15-29	195	79	40.5	200	68	34.0	395	147	37.2
30-59	173	64	37.0	170	65	38.2	343	129	37.6
60+	47	18	38.3	37	20	54.1	84	38	45.2
Total	657	257	39.1	630	237	37.6	1287	494	38.4

Annex 1.2 Durations of each movement over 15 months.



Mae Hong Son, Thailand, 1990-1991.

Annex 1.3 Details of activities.

Activities	No. of Movements	(%)	No. of person-nights	(%)	Coding
01	830	44.2%	7664	39.7%	01 = Farming, harvesting
02	17	0.9%	260	1.3%	02 = Looking after animals
03	163	8.7%	2111	10.9%	03 = Follow parents or spouse
04	5	0.3%	62	0.3%	04 = Trading
05	149	7.9%	2041	10.6%	05 = Logging
06	46	2.4%	190	1.0%	06 = Taking care of children
07	40	2.1%	389	2.0%	07 = Sick and staying in a hospital
08	56	3.0%	997	5.2%	08 = Education, training, monkhood
09	290	15.4%	2025	10.5%	09 = Visiting relatives
10	56	3.0%	942	4.9%	10 = Unskilled labour
11	53	2.8%	808	4.2%	11 = Working for reforestation projects
12	12	0.6%	302	1.6%	12 = Skilled labour
13	25	1.3%	67	0.3%	13 = Cultural or religeous ceremony
14	2	0.1%	21	0.1%	14 = Teaching
15	53	2.8%	492	2.5%	15 = Soldier, border or forest petrolling
16	16	0.9%	45	0.2%	16 = Shopping
17	23	1.2%	63	0.3%	17 = Entertaining
18	2	0.1%	31	0.2%	18 = Driving, not related to logging
19	9	0.5%	59	0.3%	19 = Catching mosquitoes
20	10	0.5%	57	0.3%	20 = Working in health posts or government offices
25	19	1.0%	680	3.5%	25 = Others
99	2	0.1%	8	0.0%	99 = Unknown
Total	1878	100.0%	19314	100.0%	

21 = Hunting, fishing (Late night activity), total number = 69 haft nights;

Recoding

1 - Agriculture	01,02
2 - Forest activities	05,11,15
3 - Kin visiting	09
4 - Followers	03
5 - Education,Religious,Entertain,Illness	06,07,08,13,17
6 - Others	04,10,12,14,16,18,19,20,25,99

see details after recoding in text (Table 3.3).

Annex 1.4 Other mosquito biting protecting methods.

Other individual protecting methods	Number of movements, by whether a net taken			Total
	No	Yes	Unknown	
None	4	43	3	50
Fire	380	231	6	617
Mosquito coils	1	1	0	2
Blanket	328	589	43	960
Unknown	33	74	142	249
Total	746	938	194	1,878

Annex 1.5 Malaria cumulative risks, by type of movement[1].

a) Number of activity involved

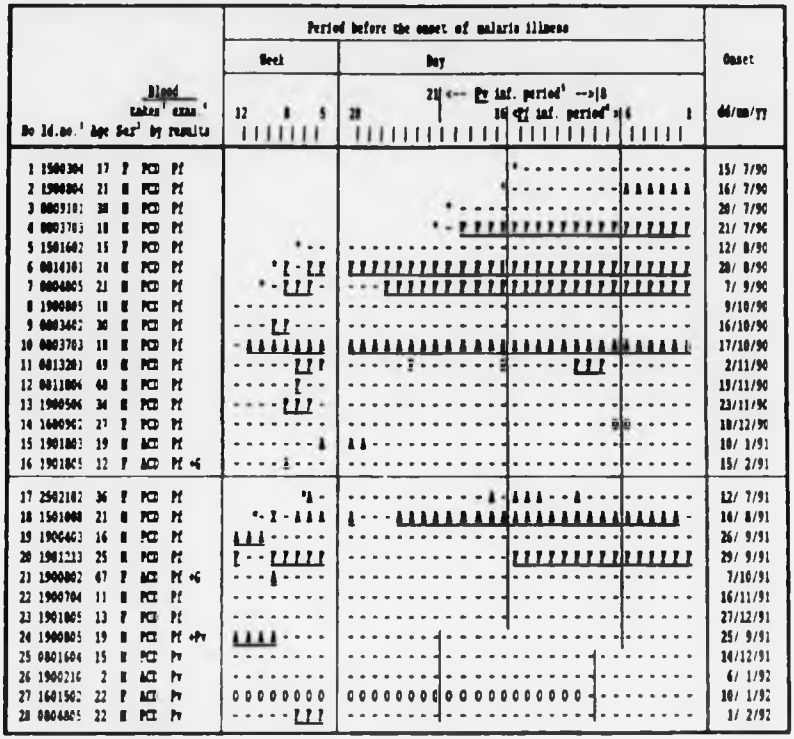
	Number of		Cumulative	Risk
	Persons	Cases	risk (%)	ratio
Person with no movement	130	2	1.5	1.0
Person always involved in only 1 type of activity	171	7	4.1	2.7
Person involved in >1 types of activity	193	15	7.8	5.1
Total	494	24	4.9	$p<0.01^{t}$

b) Detailed activity involved

Type of activity	Number of		Cumulative	Risk
	Persons	Cases	risk (%)	ratio
Person with no movement	130	2	1.5	1.0
Person always involved in only 1 activity:				
Agricultural	79	2	2.5	1.7
Forest	8	2	25.0	16.3*
Others	84	3	3.6	2.3
Person involved in > 1 activities:				
Forest + others	62	8	12.9	8.4**
Others	131	7	5.3	3.5
Total	494	24	4.9	

[1] - Malaria cumulative risks over 15 months of the study;
t - Chi-square test for a linear trend;
* - Chi-square test is significant at $p < 0.05$;
** - Chi-square test is significant at $p < 0.01$;
*** - Chi-square test is significant at $p < 0.005$;

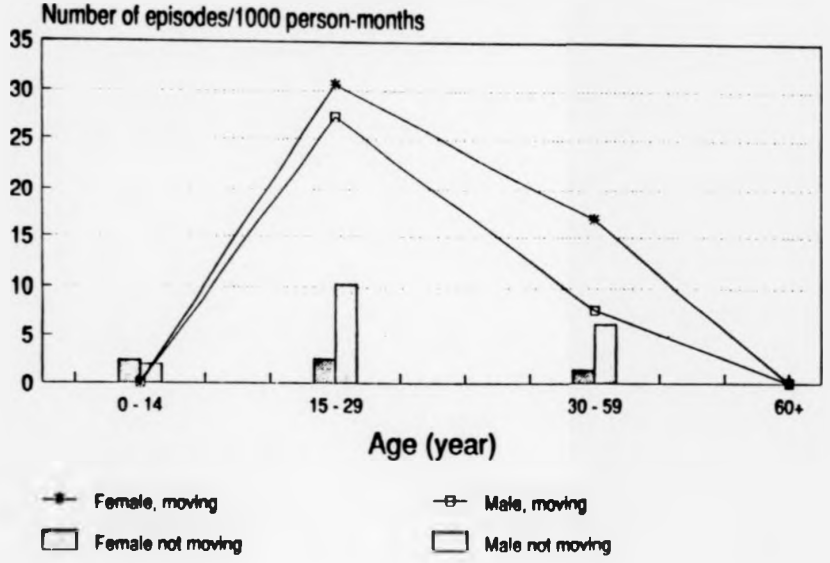
Annex 1.6 Details of movements among cases.



1) Id.no. - Identification number;
2) M - Male; F - Female;
3) PCD - Passive case detection system; ACD - Active case detection system;
4) Pf - Plasmodium falciparum; G - Falciparum gametocyte;
Pv - Plasmodium vivax;
5) The usual infected period for P.vivax - This corresponds with the incubation period of 9 - 28 days.;
6) The usual infected period for P.falciparum - This corresponds with the incubation period of 7 - 15 days.;

* - The beginning of a cohort;
\- - Staying in the village;
A - Agricultural activities (farming, looking after cattle, harvesting);
Ā - Agricultural activities with a bed net was taken along;
F - Forest activities (logging, reforestation, military service, hunting);
F̄ - Forest activities with a bed net was taken along;
O - Other activities (following parents, his visits, education, entertainments, labours, and other sociocultural activities);
N - Late night activities (hunting, fishing in the forest near the village);

Annex 1.7 Malaria incidence rate, by age sex and movement.



Annex 1.8 Malaria incidence rates, by distance and activity of movement.

Distance (km)	Acitivity Agriculture	Forest	Others	Total
0 - 2				
episodes	1	0	0	1
person-nights at risk	1,924	5	548	2,477
*Incidence rate	15.6	-	-	12.1
3 - 30				
episodes	2	2	1	5
person-nights at risk	5,729	906	4,488	11,123
Incidence rate	10.5	66.2	6.7	13.5
≥ 30				
episodes	0	2	1	3
person-nights at risk	193	2,020	2,741	4,954
Incidence rate	-	29.7	10.9	18.2
Unknown				
episodes	0	1	0	1
person-nights at risk	78	410	272	760
Incidence rate	-	73.2	-	39.5

*Incidence rate - A number fo episodes/ 1,000 person-nights.

Annex 1.9 Malaria incidence rates, by shelter type and activity of movement.

Type of shelter	Acitivity Agriculture	Forest	Others	Total
Permanent				
episodes	0	0	2	2
person-nights at risk	623	814	5,895	7,332
*Incidence rate	-	-	10.2	8.2
Semi-permanent				
episodes	3	4	0	7
person-nights at risk	7,148	2,015	666	9,829
Incidence rate	12.6	59.6	-	21.4
Temporary				
episodes	0	0	0	0
person-nights at risk	89	440	3	532
Incidence rate	-	-	-	-
Unknown				
episodes	0	1	0	1
person-nights at risk	64	72	1,485	1,621
Incidence rate	-	416.7	-	18.5

*Incidence rate - A number fo episodes/ 1,000 person-nights.

Annex 1.10 Person-nights of moving, by age, whether a net was taken and activity.

Agricultural activity

AGE(yr)	A net taken: Yes	No	Unk	Total
0-14	354	319	67	740
	47.8%	43.1%	9.1%	9.3%
15-29	1593	653	108	2354
	67.7%	27.7%	4.6%	29.7%
30-59	2846	796	174	3816
	74.6%	20.9%	4.6%	48.2%
60+	727	255	32	1014
	71.7%	25.1%	3.2%	12.8%
Total	5520	2023	381	7924
	69.7%	25.5%	4.8%	

Forest activity

AGE(yr)	A net taken: Yes	No	Unk	Total
0-14	20	1	0	21
	95.2%	4.8%	0.0%	0.6%
15-29	2338	138	0	2476
	94.4%	5.6%	0.0%	74.1%
30-59	536	224	15	775
	69.2%	28.9%	1.9%	23.2%
60+	37	29	3	69
	53.6%	42.0%	4.3%	2.1%
Total	2931	392	18	3341
	87.7%	11.7%	0.5%	

Kin visiting

AGE(yr)	A net taken: Yes	No	Unk	Total
0-14	1	77	3	81
	1.2%	95.1%	3.7%	4.0%
15-29	134	1101	33	1268
	10.6%	86.8%	2.6%	62.6%
30-59	3	482	4	489
	0.6%	98.6%	0.8%	24.1%
60+	0	184	3	187
	0.0%	98.4%	1.6%	9.2%
Total	138	1844	43	2025
	6.8%	91.1%	2.1%	

Follower

AGE(yr)	A net taken: Yes	No	Unk	Total
0-14	232	124	1505	1861
	12.5%	6.7%	**80.9%**	88.2%
			99.3%	
15-29	72	168	10	250
	28.8%	67.2%	4.0%	11.8%
30-59	0	0	0	0
60+	0	0	0	0
Total	304	292	1515	2111
	14.4%	13.8%	71.8%	
			100.0%	

(Annex 1.10 continued)

Sociocultural activities

AGE(yr)	A net taken Yes	No	Unk	Total
0-14	294	458	8	760
	> 38.7%	60.3%	1.1%	> 44.5%
15-29	386	229	143	758
	> 50.9%	30.2%	18.9%	> 44.4%
30-59	2	109	16	127
	> 1.6%	85.8%	12.6%	> 7.4%
60+	4	57	0	61
	> 6.6%	93.4%	0.0%	> 3.6%
Total	686	853	167	1706
	40.2%	50.0%	9.8%	

Miscellaneous

AGE(yr)	A net taken Yes	No	Unk	Total
0-14	36	249	5	290
	> 12.4%	85.9%	1.7%	> 13.1%
15-29	407	903	140	1450
	> 28.1%	62.3%	9.7%	> 65.7%
30-59	78	370	3	451
	> 17.3%	82.0%	0.7%	> 20.4%
60+	0	13	3	16
	> 0.0%	81.3%	18.8%	> 0.7%
Total	521	1535	151	2207
	23.6%	69.6%	6.8%	

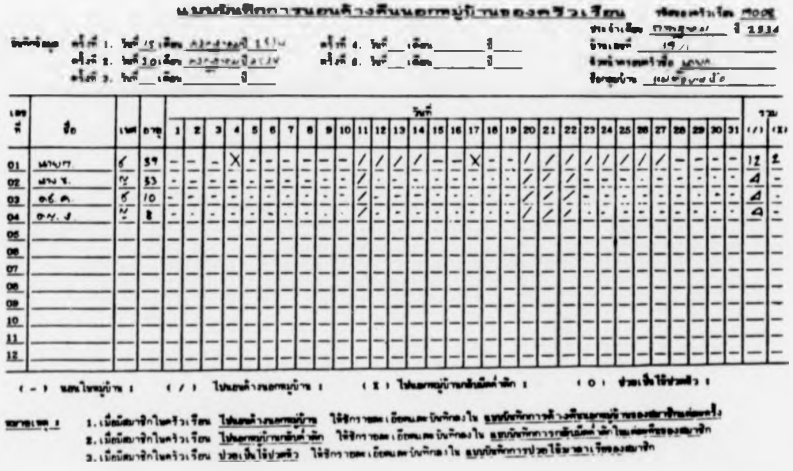
Annex 1.11 Details of forms and questionnaires.

a) Movement monitoring form

1st visiting date..... Household code.....
2nd visiting date..... Month.....
3rd visiting date..... Head of household.....
Address.....

No.	Name	Sex	Age	Date 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Total /	X

(-) staying in residence;
(/) overnight absence; Recording details on a form for an overnight absence.
(X) late night movements; Recording details on a form for a late night movement.
(O) fever; Recording details on a form for a fever.



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b) Structured questionnaire for an overnight absence (/)

Use this form for each absentee and each absent period.

1. Household code_____	_ _ _ _ _	[1-5]
2. Head of hosehold_____		
3. Id.no._____	_ _	[6-7]
4. Name _____		
5. sex ____	_	[8]
6. Age_____	_ _	[9-10]
7. Where did the absentee go to ?		
_____		
8. How far the place from the village ? _____km.	_ _	[11-12]
9. What was the reason for ? _____	_ _	[13-14]
_____		
10. Date of the absence _ _/_ _/ _ _	_ _/ _ _/ _ _	[15-20]
11. The returning date _ _/_ _/ _ _	_ _/ _ _/ _ _	[21-26]
12. The type of shelter during moving	_	[27]
_____		
13. What were the mosquito protecting methods ?	_	[28]
_____		
14. Was a bednet taken ?	_	[29]
1. Yes, but the use was not known.		
2. Yes, and it was used.		
3. Yes, but it was not used.		
4. No, it was not taken.		
9. Not known.		
15. Name of the interviewer. _____	_	[30]
16. Date of recording. _ _/ _ _/ _ _	_ _/ _ _/ _ _	[31-36]
17. The informant. _____	_	[37]

c) Structured questionnaire for a late night movement (X)

Use this form for each mover and each movement.

1. Household code_____	_ _ _ _ _	[1-5]
2. Head of hosehold_____		
3. Id.no._____	_ _	[6-7]
4. Name _____		
5. sex ____	_	[8]
6. Age_____	_ _	[9-10]
7. Where did the mover go to ?		
_____		
8. How far the place from the village ? _____km.	_ _	[11-12]
9. What was the reason for ? _____	_ _	[13-14]
_____		
10. Date of the movement _ _/_ _/_ _ _	_ _/_ _/_ _ _	[15-20]
11. The returning time _ _	_ _	[21-22]
12. What were the mosquito protecting methods ?	_	[23]
_____		
13. Name of the interviewer. _____	_	[30]
14. Date of recording. _ _/_ _/_ _ _	_ _/_ _/_ _ _	[31-36]
15. The informant. _____	_	[37]

d) Strucutred questionnaire for fevers (**O**)

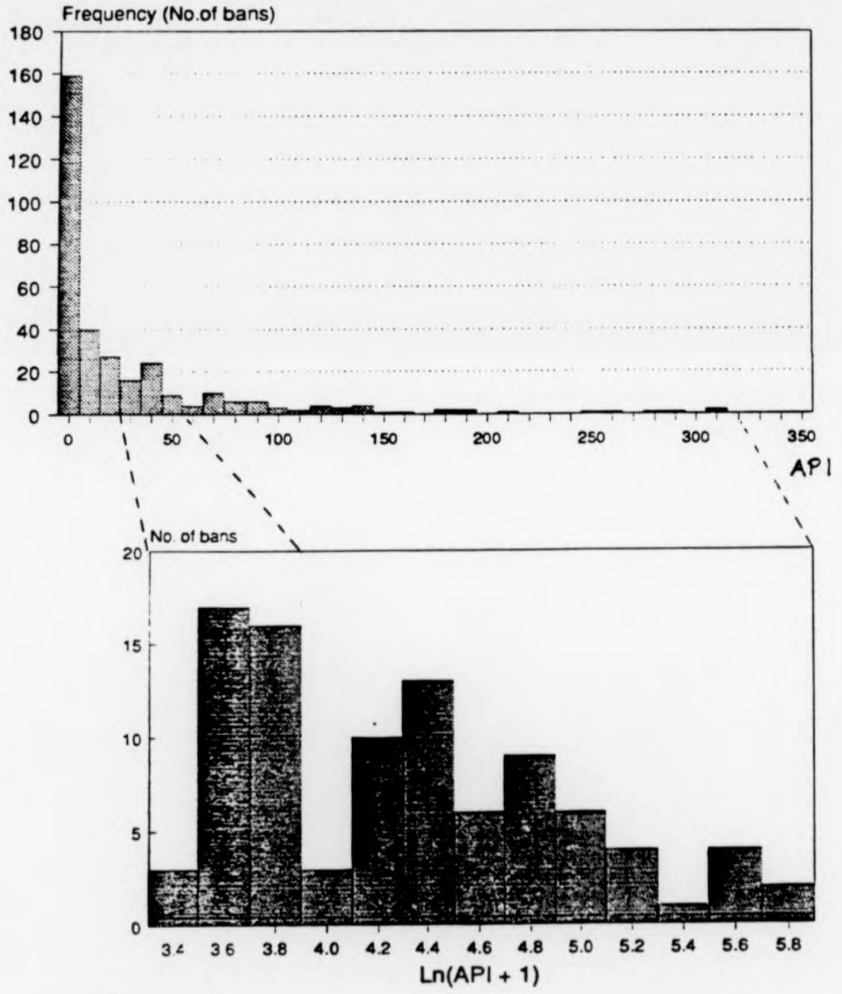
Use this form for each illness.

1. Household code_____	_ _ _ _ _	[1-5]
2. Head of hosehold_____		
3. Id.no._____	_ _	[6-7]
4. Name _____		
5. sex ____	_	[8]
6. Age_____	_ _	[9-10]
7. Date of the illness _ _/_ _/_ _ _	_ _/_ _/_ _ _	[15-20]
8. Name of the interviewer. _____	_	[30]
9. Date of recording. _ _/_ _/_ _ _	_ _/_ _/_ _ _	[31-36]
10. The informant. _____	_	[37]

ANNEX 2

Details on the impregnation trial

Annex 2.1 The distribution of the annual incidence rate in each ban and their natural logarithmic transformation.



Mae Sanang district. 1989.

Annex 2.2 The sample size calculation.

The logarithmic transformed annual rate in each ban was used as a basis for sample size calculation. Its distribution was assumed to be the Normal Distribution. The sample size to detect a mean difference between the intervention and control groups was calculated as follow (Smith and Morrow, 1991):

$$n = \frac{(Z_1 + Z_2)^2 * (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

n = Number of bans in each group

σ_i = Standard deviation in group$_i$

μ_i = Mean in group$_i$

Z_1 = 1.96 for 95% precision

Z_2 = 1.28 for 90% power or 0.84 for 80% power

The expected difference between means of the annual rates in both group is at least 50%. Hence, on the natural logarithmic scale, $\mu_1 - \mu_2 = \ln(2) = 0.693$. Assuming that $\sigma_1 = \sigma_2$ = s.d., then

$$n = \frac{(Z_1 + Z_2)^2 * 2(\text{s.d.})^2}{(0.693)^2}$$

$= 43.8 * (\text{s.d.})^2$ for 90% power or

$= 32.6 * (\text{s.d.})^2$ for 80% power

With the annual rates higher than 30 episodes/1,000 persons/year, the s.d. on the natural logarithmic scale = 0.62, hence, $n = 17$ bans for 90% power or 13 bans for 80% power.

With the annual rates higher than 50 episodes/1,000 persons/year, the s.d. on the natural logarithmic scale = 0.47,

hence, $n = 10$ bans for 90% power or 8 bans for 80% power.

Annex 2.3 Details of bednet funds, and sizes, materials and prices of bednets distributed.

The bednet fund scheme has been developed by the Malaria Centre II, Chiang Mai since 1986. There were 4 funds in the study area before the study started in 1990. The research team enhanced this scheme by making the following agreements with the communities.

1. The bednet fund was a community fund at ban level managed by the ban committee under the supervision of a teacher or malaria worker.

2. The fund provided bednets to villagers in subsidised prices and on a deposit payment basis.

3. The research team was responsible for surveying size and number of bednets required, with the coordinated help of the ban committee. Bednets needed were given by the research team to the fund.

4. The fund distributed bednets and collected the deposits.

5. The money was kept and managed by the fund committee for further purchase of new bednets.

6. The subsidised price were set as follow:

Nylon bednet, small size (No.4)	$1.6 /net
Nylon bednet, medium size (No.5)	$2.0 /net
Nylon bednet, large size (No.7)	$2.8 /net
Polycotton bednet, small size (No.3)	$2.0 /net
Polycotton bednet, small size (No.4)	$3.6 /net
Polycotton bednet, medium size (No.5)	$4.0 /net
Polycotton bednet, medium size (No.6)	$4.4 /net

Polycotton bednet, large size (No.7) $4.8 /net

Polycotton bednet, large size (No.8) $5.2 /net

A polycotton bednet is made from the cotton and synthetic threads interwoven together. The raw net materials were bought from the market in Chiang Mai and sent to malaria sectors in the district for sewing by the wife of the malaria sector headmen.

Annex 2.4 Studies on the mass dipping methods and dosages.

2.4.1 Objective

The objective for these studies was to develop a simple way for mass treating bednets which could be effectively handled by the community.

2.4.2 Assumption

The amount of insecticide on a treated net depends on the amount of the aqueous insecticide solution needed to just wet the net. The latter depends on the amount of water which just saturates the net. This amount depends on the net material. With the same materials, nets with different sizes should take up the same amount of water and insecticide per square metre. Hence, the proper dilution of 5% emulsified concentrated lambda-cyhalothrin to achieve the target dosage of 10 mg/m^2 depends on the amount of water per a square metre for each material. This allows many nets to be dipped in the same container, assuming that the target dosage is directly related to the amount of aqueous insecticide solution which just saturates the net. The remaining solution in the container has the same concentration as the solution soaked up by the nets.

2.4.3 Mass dipping method development

2.4.3.1) The amount of water which just saturates a net

After dipping, squeezing and hanging up a wet nylon net, there is still a considerable amount of excess water collecting at the lowest part and pouring down. For a wet cotton net, this process is very slow with only a few drops running down. Table 2.4.1 shows the amount of water, as cc/m^2, remaining on wet nylon nets after they are squeezed. The rate of excess water pouring down is high during the first 5 minutes and very low after 20 minutes.

Table 2.4.1 The amount of water on nylon nets 5 and 20 minutes after being dipped, squeezed and hung up.

Nylon net number	The amount of water on nets ($cc./m^2$)		
	immediately after wringing	after hanging for 5 minutes	after hanging for 20 minutes
1	39.6	29.0	21.0
2	31.5	29.2	22.5
3	-	29.0	22.3
4	35.2	27.5	21.8
mean	35.4	28.7	21.9
(s.d.)	(4.1)	(0.8)	(0.7)

2.4.3.2) 5-minute dipping process

To make the dipping process short, simple and economic, we dipped, wrung, and hung the net for 5 minutes and squeezed the excess water out again. The net was then put into a plastic bag ready for drying. The excess solution could be used to dip other nets again providing that it is not too dirty. In the case of dipping in the insecticide solution, this method can keep the excess solution for reuse, assuming that the excess solution still has a similar concentration to the original. The amount of water remaining on cotton and nylon nets after being dipped through this process was recorded. It was found that cotton nets of various sizes and materials

soaked up to 3.4 times more water than did the nylon ones. The results enabled us to estimate the proper dilution of the 5% EC lambda- cyhalothrin, targeting at a dosage of 10 mg/m^2, for mass dipping in the field.

Table 2.4.2 The amount of water (cc./m^2) remaining on nylon and cotton nets of various sizes and materials after the 5-minute dipping process.

	Remaining amount of water on the net (cc/m^2)		Expected dosages (mg/m^2) with aqueous solution	
	Nylon net	Cotton and polycotton net	Nylon net (1:100 dilution)	Cotton and polycotton net (1:300 dilution)
Total nets	14	27	14	27
mean	24.5	83.7	12.2	14.0
s.d.	1.5	11.8	0.75	1.98
95% c.i.	21.3-27.7	59.4-108.0	10.6-13.8	9.9-18.0

Assuming that similar materials should take up similar amounts of insecticide from the same insecticide solution, the amount should directly relate to the amount of solution soaked up. Two separate insecticide solutions were prepared for nylon and cotton nets according to their water uptake properties. To target at 10 mg/m^2, nylon nets were dipped in the 1:100 solution of 5% EC lambda-cyhalothrin in water (equal to 0.5 mg. of this insecticide in a cc. of the solution) and cotton nets in the 1:300 solution (equal to 0.167 mg. of the insecticide in a cc. of the solution). These were simple diluting formulas and allowed for a 95% confident range not less than the target dosage (see Table 2.4.2). This method was tested at the pilot area. The nets dipped in the laboratory room and at the pilot area were cut into two pieces for each net and a total of 12 pieces were sent to the Imperial Chemical Industry Company, England for measuring the actual dosages on the nets.

2.4.4 Pilot study

Because of the limited budget, the pilot study was aimed at testing the net distribution and mass dipping method. A Karen ban in another area was chosen for

these purposes. In this ban, there were 162 persons in 46 households; 5-9 cases per year and 46 cotton nets already existed in the ban.

2.4.4.1 Distribution of nets

A village committee was informed and asked for their cooperation in surveying the existing nets and needs for new nylon nets of each household. The total of 49 new nets was needed. The village bednet fund was set up and received 49 new nylon nets. The fund sold them on deposit and at a cheap price to those households which needed them. It also looked after the money and used it for replacing torn nets through the same deposit system.

2.4.4.2 Mass dipping of villager nets

In December 1989, all old cotton and new nylon nets in the pilot village were dipped in 5% EC lambda-cyhalothin solution targeting at 10 mg/m^2 by the 5-minute dipping method mentioned. Villagers did not comply with instructions to dry treated nets by laying them down in the shade, but dried them as they liked. Most of them hung wet nets up to dry. Villagers were encouraged not to wash their treated nets until the next impregnation.

2.4.4.3 Side-effect of the treated nets

Two weeks later, key persons were interviewed about the good and bad things regarding the use of treated nets. They presented a very high preference for the treated nets because of its odourlessness and simplicity. Some Karens complained of sneezing and running nose for few days after the impregnation but still preferred it to DDT spraying. They were willing to have their nets dipped again.

2.4.5 Actual dosage study

Results of the gas-liquid chromatographic analysis of 12 pieces of nets were available from ICI, England. This enabled us to assess our dipping method. Table 2.4.3 shows that the uptake rates of cotton nets are about 2-3 times less than those of nylon ones.

Table 2.4.3 Actual dosages and uptake rates.

Net characteristics (surface area, m^2)	Dipping concentration (Drying method)	Remaining water (cc/m^2)	Target* dosage (mg/m^2)	Actual** dosage (mg/m^2)		Uptake*** rate (%)
1) New polycotton net ($13.79\ m^2$)	0.14 mg/cc. (laying)	86.66	12.13	H	3	25
				L	3	25
2) Old cotton net ($11.28\ m^2$)	0.14 mg/cc. (laying)	67.38	9.43	H	3	32
				L	4	42
3) New nylon net ($14.20\ m^2$)	0.4 mg/cc. (laying)	24.79	9.92	H	6	60
				L	8	81
4) New nylon net ($14.25\ m^2$)	0.4 mg/cc. (hanging)	25.47	10.19	H	8	79
				L	10	98
5) New nylon net ($14.40\ m^2$)	1 mg/cc. (laying)	21.18	21.18	H	12	57
				L	15	71
6) New nylon net ($13.91\ m^2$)	0.5 mg/cc. (laying)	25.40	12.7	H	9	71
				L	12	94

* - target dosage = remaining water (cc/m^2) * dipping concentration (mg/cc);
** - measured by the gas-liquid chromatographic method by ICI laboratory;
*** - uptake rate (%) = the actual dosage * 100/ the target dosage;
H - a piece cut from the highest part of a treated net;
L - a piece cut from the lowest part of a treated net.

2.4.6 Bioassay study in the pilot area

The villager nets in the pilot area were taken back periodically after dipping in December 1989 for bioassay testing. The used treated nets were tested by exposing mosquitoes to them for 3 minute and the 24 hour mortality rate (%) recorded. These were done by Mr.Pradya Somboon, a PhD student in entomology. The results showed that these nets were effective for at least 5-7 months (Table 2.4.4).

Table 2.4.4 Bioassays of impregnated bednets from the pilot area.

Bed net no.	Types of net	Month of use	% 24 hr mortality after 3 min. exposure*		
			test1	test2	average
1	cotton	5	100	100	100
2	cotton	5	100	100	100
3	cotton	5	100	100	100
4	nylon	5	100	100	100
5	nylon	5	100	100	100
control	nylon	0	0	0	0
6	nylon	7	100	70	85
7	nylon	7	90	70	80
8	cotton	7	100	100	100
9	cotton	7	100	100	100
control	nylon	0	10	0	5
10	nylon @	9	90	80	85
11	nylon	9	100	90	95
12	nylon	9	40	50	45
13	cotton	9	50	0	25
14	cotton #	9	30	20	25
15	cotton	9	0	0	0
control	nylon	0	10	0	5

* Ten mosquitoes were used in each test.
@ washed once with water
# washed twice with detergent

Annex 2.5 Sleeping time and use of bednet.

a) Analysis by ban.

Ban No.	Number of person-nights	7+	8+	9+	10+	11+	12+	1+	2+	3+	4+	5+	6+
		p.m.						a.m.					
15	(Total 151 person-nights)												
	Go to bed	9	74	100	110	126	129	128	126	126	122	96	26
	(%)	(6)	(49)	(66)	(80)	(83)	(86)	(85)	(83)	(86)	(81)	(64)	(17)
	- sleep under a net	8	58	78	98	105	107	108	105	104	100	81	25
	- not sleep under a net	1	16	22	22	21	22	20	21	22	22	15	1
25	(Total 108 person-nights)												
	Go to bed	3	45	82	91	96	94	92	95	95	75	43	2
	(%)	(3)	(42)	(76)	(84)	(89)	(87)	(85)	(88)	(88)	(69)	(40)	(2)
	- sleep under a net	3	25	43	45	46	44	45	45	44	36	19	2
	- not sleep under a net	0	20	39	46	50	50	47	50	51	39	24	0
Total 259 person-nights													
	Go to bed	12	119	182	211	222	223	220	221	221	197	139	28
	(%)	(5)	(46)	(70)	(82)	(86)	(86)	(85)	(85)	(85)	(76)	(54)	(11)

b) Analysis by sex.

Sex	Number of person-nights	7+	8+	9+	10+	11+	12+	1+	2+	3+	4+	5+	6+
		p.m.						a.m.					
Male	(Total 135 person-nights)												
	Go to bed	4	58	89	105	115	115	113	113	113	102	84	21
	(%)	(3)	(43)	(66)	(78)	(85)	(85)	(84)	(84)	(84)	(76)	(62)	(16)
	- sleep under a net	4	41	55	66	74	72	73	72	70	65	58	21
	- not sleep under a net	0	17	34	39	41	43	40	41	43	37	26	0
Female	(Total 124 person-nights)												
	Go to bed	8	61	93	106	107	108	107	108	108	95	55	7
	(%)	(6)	(49)	(75)	(82)	(86)	(87)	(86)	(87)	(87)	(77)	(44)	(6)
	- sleep under a net	7	42	66	77	77	79	80	78	78	71	42	6
	- not sleep under a net	1	19	27	29	30	29	27	30	30	24	13	1

c) Analysis by age group.

Age (year)	Number of person-nights	p.m. 7+	8+	9+	10+	11+	12+	a.m. 1+	2+	3+	4+	5+	6+
0-9	(Total 69 person-nights)												
	Go to bed	7	57	66	68	68	68	68	68	67	63	54	46
	(%)	(10)	(83)	(96)	(99)	(99)	(99)	(99)	(99)	(97)	(91)	(78)	(23)
	- sleep under a net	6	40	45	46	46	46	46	46	45	42	40	16
	- not sleep under a net	1	17	21	22	22	22	22	22	22	21	14	0
10-29	(Total 117 person-nights)												
	Go to bed	2	30	63	79	85	86	84	86	88	80	57	4
	(%)	(2)	(26)	(54)	(68)	(73)	(74)	(72)	(74)	(75)	(68)	(49)	(3)
	- sleep under a net	2	21	40	51	54	55	56	55	56	56	37	4
	- not sleep under a net	0	9	23	28	31	31	28	31	32	24	20	0
39-55	(Total 68 person-nights)												
	Go to bed	3	29	49	59	64	65	63	62	61	49	25	8
	(%)	(4)	(43)	(72)	(87)	(94)	(96)	(93)	(91)	(90)	(72)	(37)	(12)
	- sleep under a net	3	19	32	41	46	46	46	44	42	33	20	7
	- not sleep under a net	0	10	17	18	18	19	17	18	19	16	5	1

Annex 2.6 Activities out of bednets.

Number of person-nights	p.m. 7+	8+	9+	10+	11+	12+	a.m. 1+	2+	3+	4+	5+	6+
(Total 259 person-nights)												
Within the household	177	69	22	10	1	4	1	0	5	24	77	195
Around the household	9	6	5	2	3	2	0	7	6	11	19	12
Within the ban	23	30	14	2	0	0	0	0	0	0	0	2
Out of the ban	38	35	36	34	33	30	30	31	27	27	24	22
Total	247	140	77	48	37	36	31	38	38	62	120	231
(%)	(95)	(54)	(30)	(19)	(14)	(14)	(12)	(15)	(15)	(24)	(46)	(89)

Annex 2.7 Relationship between the incidence rate and the density of bednets.

Ban no.	NET[1]	No. of[2] persons/net	Incidence[3] rate	Log_e of (rate + 1)
01	1	1.79	18.3	2.96
02	1	2.12	59.2	4.10
03	1	1.80	48.7	3.91
04	1	1.96	20.8	3.08
05	1	1.42	34.5	3.57
09	1	1.79	11.9	2.56
07	2	2.17	47.2	3.88
15	1	2.02	55.5	4.03
08	2	2.32	31.1	3.47
16	1	1.48	45.4	3.84
06	1	1.21	42.7	3.78
10	1	0.98	37.3	3.64
11	2	4.21	32.7	3.52
12	2	3.39	26.0	3.30
17	2	3.30	49.5	3.92
18	2	2.32	58.0	4.08
19	2	2.65	130.8	4.88
25	2	4.40	71.3	4.28
20	2	2.54	68.9	4.25
23	2	4.09	77.1	4.36
21	1	2.44	38.7	3.68
22	1	2.48	51.6	3.96
13	2	3.83	223.3	5.41
24	2	6.36	106.0	4.67

1 - 1 = Receiving untreated bednets through bednet funds in May 1990,
2 = No additional bednets received from the researchers.

2 - Estimated from the second census data collected during September to November 1990.

3 - Malaria illness incidence rate during 8 month period after the distribution of untreated bednets, standardised by age and sex.

Regression of the log_e(rate + 1) on the number of persons/net

Correlation coefficient: $r = 0.48$

$r^2 = 0.23$

95% confidence limits: $0.10 < R < 0.74$

Source	df	Sum of Squares	Mean Square	F-statistic	p value
Regression	1	8.1959	8.1959	6.65	<0.05
Residuals	22	27.1219	1.2328		
Total	23	35.3178			

B Coefficients

Variable	Mean	B coefficient	95% confidence Lower	Upper	Partial Std Error	F-test
LN(API)	3.8804	0.9716974	0.233049	1.710345	0.376861	6.6481
Y-Intercept		-1.1426741				

Annex 2.8 Summary of age- and sex-adjusted incidence rate ratios.

a) Natural logarithmic values of the age- and sex-adjusted rate ratios (Icon/placebo) and their statistics.

Pair No.	12 months before dipping	8 months after 1st dipping	8 months after 2nd dipping	Total 16 months after dipping
01	0.9266	1.9144	-0.6170 (4)[3]	0.8509 (9)[3]
02	0.4971	1.0478	-1.4100 (9)	-0.1178 (1)
03	-1.4680	-0.7280	-3.1800 (11)	-0.9895 (10)
04	0.0966	-0.3240	-0.9490 (6)	-0.6244 (8)
05	0.4393	-2.4980	-0.5980 (3)	-1.0544 (11)
06	0.2216	-0.1490	2.8779 (10)	0.4921 (6)
07	1.1310	-0.7760	-0.4130 (1)	-0.6017 (7)
08	-0.1560	0.4655	-1.2320 (8)	-0.2835 (3)
09	-0.7850	-0.4350	-3.6290 (12)	-1.0944 (12)
10	-0.2920	2.7161	-0.7750 (5)	-0.2135 (2)
11	-0.0910	0.0000	0.4524 (2)	0.4524 (5)
12	-0.5310	0.8232	-1.0690 (7)	-0.3516 (4)
mean	-0.0009	0.1714	-0.8785	-0.2946
sd.	0.7266	1.3608	1.6395	0.6348
SE [1]	0.2098	0.3928	0.4733	0.1833
1.96*SE [2]	0.4112	0.7699	0.9277	0.3593
mean+1.96*SE	0.4103	0.9413	0.0492	0.0647
mean-1.96*SE	-0.4121	-0.5985	-1.8062	-0.6539
e^{mean}	0.9991	1.1870	0.4154	0.7448
$e^{mean+1.96*SE}$	1.5073	2.5633	1.0504	1.0668
$e^{mean-1.96*SE}$	0.6623	0.4960	0.1643	0.5200
t score	-0.0043	0.4364	-1.8561 (T_+=12)[4]	-1.6076 (T+=20)
p value	>0.50	n.s.	<0.10 (<0.05)[5]	<0.15 (n.s.)

1 - SE = sd./√n , n = 12
2 - t = 2.2010
(critical t value at 2α = 0.05 and degree of freedom = 11).
3 - Rank value for Wilcoxon signed-rank test.
4 - T_+ = sum of rank values with positive difference
= sum of rank value of pair no.6 and 11
= 10 + 2
(T = 66)
5 - 5% critical value at n = 12: the small T ≤13
2% critical value at n = 12: the small T ≤ 9

b) Summary of logarithmic and converted age- and sex-specific rate ratios

	Average of $\log_e$(Rate ratio $_{Icon/Placebo}$)			Converted rate ratio		
	Male	Female	Summary	Male	Female	Summary
12 months before the intervention						
agegr 0-14	0.023	-0.737		1.023	0.479	
15+	-0.610	0.574		0.543	1.775	
Summary	-0.353	-0.106	-0.001	0.703	0.899	**0.999**
8 months after the first impregnation						
agegr 0-14	-0.131	0.252		0.877	1.287	
15+	-0.786	0.506		0.456	1.659	
Summary	-0.196	0.488	0.171	0.822	1.629	**1.187**
8 months after the second impregnation						
agegr 0-14	-0.530	-0.609		0.589	0.544	
15+	-2.465	-0.185		0.085	0.831	
Summary	-1.696	-0.426	-0.878	0.183	0.653	**0.415**
Total 16 months after 2 impregnations						
agegr 0-14	-0.551	-0.078		0.576	0.925	
15+	-1.657	0.320		0.191	1.377	
Summary	-0.989	0.253	-0.294	0.372	1.288	**0.745**

c) Analysis of $\log_e$(rate ratio$_{\text{Icon/placebo}}$) by age and sex.

MALE

	0-14							15+						
	Larr(I/P)				Diff1/0	Diff2/0		Larr(I/P)				Diff1/0	Diff2/0	
Pairno	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0
01	1.95253	0	0.6082	0.60821	-1.9525	-1.3463	-1.344	0.33443	2.5840	-3.857	0.62650	2.24957	-4.1921	0.2920
02	0.11640	-2.546	-0.022	-0.3033	-2.6630	-0.1390	-0.419	0.82507	1.2109	-3.904	0.03958	0.38590	-4.7292	-0.785
03	-4.7194	-0.259	0	-0.2593	4.46009	4.71949	4.4600	-3.8840	-4.543	-4.259	-5.0985	-0.6595	-0.3753	-1.214
04	0.47920	0	0	0	-0.4792	-0.4792	-0.479	-0.3102	-0.347	-3.536	-1.0259	-0.0372	-3.2258	-0.715
05	1.01233	0	-2.211	-2.2115	-1.0123	-3.2239	-3.223	-0.1306	-3.278	-3.867	-4.2951	-3.1477	-3.7365	-4.164
06	3.47351	0	0	0	-3.4735	-3.4735	-3.473	0.61184	0.4590	2.6625	0.67847	-0.1520	2.05154	0.0674
07	-0.2622	-3.124	-3.795	-4.1929	-2.8618	-3.5327	-3.930	-3.8840	-0.163	-4.035	-0.7448	3.72059	-0.1512	3.1391
08	-0.4756	4.3557	4.3557	5.04243	4.83114	4.83114	5.5178	0.31353	-4.462	-4.462	-5.1499	-4.7761	-4.7761	-5.463
09	0.28471	0	-4.566	-4.5668	-0.2847	-4.8515	-4.851	-0.9195	-4.491	-3.414	-4.7761	-3.5717	-2.4952	-3.856
10	-0.7896	0	3.0256	3.02567	0.78945	3.81512	3.8151	-0.1966	3.4939	-0.620	-0.0707	3.69059	-0.4238	0.1259
11	0.18132	0	0	0	-0.1813	-0.1813	-0.181	0.23819	0	0	0	-0.2381	-0.2381	-0.238
12	-0.9742	0	-3.753	-3.7534	0.97421	-2.7792	-2.779	-0.3126	0.1098	-0.286	-0.0694	0.42269	0.02662	0.2432
Mean[1]	0.02326	-0.131	-0.529	-0.5509	-0.1544	-0.5532	-0.570	-0.6096	-0.785	-2.465	-1.6571	-0.1761	-1.8554	-1.047
S.D.	1.85728	1.7097	2.5717	2.72157	2.53388	3.22471	3.3210	1.53100	2.6581	2.2026	2.29662	2.55721	2.17260	2.2652
S.E.	0.53615	0.4935	0.7423	0.78565	0.73146	0.93089	0.9587	0.44196	0.7673	0.6358	0.66297	0.73820	0.62717	0.6539
t[2]	0.04339	-0.265	-0.713	-0.7012	-0.2111	-0.5943	-0.598	-1.3793	-1.023	-3.876	-2.4996	-0.2385	-2.9584	-1.601

Female

	0-14							15+						
	Larr(I/P)				Diff1/0	Diff2/0		Larr(I/P)				Diff1/0	Diff2/0	
Pairno	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0
01	3.53611	0.4614	0	0.46148	-3.0746	-3.5361	-3.074	2.95396	1.9074	0.8441	1.56000	-1.0465	-2.1097	-1.393
02	0.60782	0	-2.767	-2.7679	-0.6078	-3.3757	-3.375	-2.7540	2.5798	-2.700	-0.1207	5.33388	0.05342	2.6332
03	-4.0352	0.6857	0	0.68573	4.72095	4.03522	4.7209	0.34215	-3.931	0	-3.9318	-4.2739	-0.3421	-4.273
04	3.71357	0	0	0	-3.7135	-3.7135	-3.713	1.18084	0	2.5252	2.52526	-1.1808	1.34442	1.3444
05	-2.2115	-2.241	0	-2.2410	-0.0294	2.21157	-0.029	2.54142	-1.652	1.7913	1.19888	-4.1938	-0.7500	-1.342
06	0	0	3.3074	3.30746	0	3.30746	3.3074	-1.3622	-3.643	3.2701	-0.1735	-2.0814	4.63248	1.1887
07	1.93332	0	0	0	-1.9333	-1.9333	-1.933	5.46507	-3.965	0.7866	-0.1125	-9.4301	-4.6784	-5.577
08	0	4.3557	-4.282	0.07312	4.35572	-4.2826	0.0731	-3.6753	4.0913	-3.638	0.45283	7.76672	0.03676	4.1281
09	-5.3033	-4.035	-4.035	-6.7194	1.26808	1.26808	0.5838	-0.5178	4.3557	0	4.35572	4.87352	0.51780	4.8735
10	-1.1796	0	0	0	1.17967	1.17967	1.1796	3.27019	2.5043	-3.753	-1.2490	-0.7658	-7.0236	-4.519
11	-4.7194	0	0.4670	0.46702	4.71949	5.18651	5.1865	0	0	0	0	0	0	0
12	-1.1867	3.7950	0	3.79500	4.98175	1.18675	4.9817	-0.5550	3.6206	-1.348	-0.6684	4.17574	-0.7930	-0.113
Mean[1]	-0.7370	0.2518	-0.609	-0.0782	0.98890	0.12782	0.6588	0.57409	0.5055	-0.185	0.31971	-0.0685	-0.7593	-0.254
S.D.	2.86145	2.1331	2.0204	2.25706	2.98562	3.20148	3.1603	2.53026	3.0012	2.1916	1.95196	4.67346	2.79282	3.2110
S.E.	0.82603	0.6157	0.5832	0.65155	0.86187	0.92418	0.9123	0.73042	0.8663	0.6326	0.56348	1.34911	0.80622	0.9269
t[2]	-0.8923	0.4089	-1.044	-0.1200	1.14738	0.13831	0.7222	0.78597	0.5835	-0.292	0.56738	-0.0508	-0.9418	-0.274

Sex-specific $\log_e$(rate ratio) adjusted by age

	Male							Female						
	Larr(I/P)				Diff1/0	Diff2/0	Diff12/0	Larr(I/P)				Diff1/0	Diff2/0	Diff12/0
Pairno	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0
01	0.72677	2.5179	-1.277	0.62420	1.79115	-2.0043	-0.102	3.28459	1.3934	0.8099	1.27584	-1.8911	-2.3946	-1.928
02	0.67153	0.9326	-1.201	-0.0447	0.26110	-1.8732	-0.716	-0.4137	2.2013	-2.724	-0.5227	2.61510	-2.3103	-0.108
03	-4.2817	-1.209	-3.818	-1.5884	3.07256	0.46310	2.6932	-0.4035	-0.198	0	-0.1988	0.20467	0.40353	0.2046
04	-0.2111	-0.340	-3.103	-1.0111	-0.1295	-2.8925	-0.800	1.54274	0	2.1488	2.14887	-1.5427	0.60612	0.6061
05	0.06752	-2.850	-3.521	-3.9144	-2.9182	-3.5886	-3.982	1.87361	-1.894	1.7132	0.79958	-3.7676	-0.1606	-1.074
06	0.75817	0.4530	2.2525	0.67045	-0.3051	1.49439	-0.087	-1.3347	-3.043	3.2830	0.23992	-1.7083	4.61782	1.5746
07	-0.8929	-0.321	-3.954	-0.9960	0.57099	-3.0619	-0.103	3.11522	0.6317	0.7788	-0.1118	-2.4835	-2.3364	-3.227
08	0.06821	-0.659	-0.659	-0.6679	-0.7276	-0.7276	-0.736	-3.2622	0.9525	-3.907	0.28230	4.19482	-0.6649	3.5245
09	-0.5484	-4.048	-3.992	-4.7054	-3.5001	-3.4442	-4.156	-1.1519	2.1288	-2.992	0.28477	3.28081	-1.8408	1.4367
10	-0.3400	3.0622	-0.389	0.06610	3.40221	-0.0499	0.4061	0.01382	0	-3.348	-1.2196	-0.0138	-3.3623	-1.233
11	0.20558	0	0	0	-0.2055	-0.2055	-0.205	-3.7151	3.6836	0.4613	0.46136	7.39879	4.17656	4.1765
12	-0.4631	0.1085	-0.688	-0.2962	0.57173	-0.2256	0.1668	-0.7718	0	-1.337	-0.4004	0.77185	-0.5661	0.3714
Mean[1]	-0.3533	-0.196	-1.696	-0.9886	0.15695	-1.3430	-0.635	-0.1069	0.4479	-0.626	0.25326	0.59490	-0.3193	0.3602
S.D.	1.28819	1.8924	1.8902	1.62469	1.95997	1.61859	1.7678	2.12291	1.7374	2.2780	0.84259	3.09937	2.61673	2.0457
S.E.	0.37187	0.5463	0.5456	0.46883	0.56579	0.46724	0.5103	0.61283	0.5015	0.6576	0.24323	0.89471	0.69765	0.5905
t[2]	-0.9501	-0.359	-3.108	-2.1087	0.27739	-2.8743	-1.244	-0.1745	0.8928	-0.648	1.04122	0.66490	-0.4577	0.6099

Summary of age- and sex-adjusted $\log_e$(rate ratio$_{Icon/placebo}$)

	Larr(I/P)				Diff1/0	Diff2/0	Diff12/0
Pairno	Before0	After1	After2	After12	Af1-Be0	Af2-Be0	A12-B0
01	0.92668	1.9144	-0.617	0.85085	0.98778	-1.5439	-0.075
02	0.49712	1.0478	-1.410	-0.1178	0.55072	-1.9071	-0.614
03	-1.6688	-0.728	-3.180	-0.9895	0.74035	-1.7120	0.4792
04	0.09660	-0.324	-0.949	-0.6244	-0.4211	-1.0460	-0.721
05	0.43930	-2.698	-0.598	-1.0544	-2.9377	-1.0380	-1.493
06	0.22163	-0.149	2.8779	0.69208	-0.3715	2.65629	0.2704
07	1.13106	-0.776	-0.413	-0.6017	-1.9078	-1.5445	-1.732
08	-0.1569	0.4655	-1.232	-0.2835	0.62253	-1.0757	-0.126
09	-0.7855	-0.435	-3.629	-1.0944	0.35048	-2.8438	-0.308
10	-0.2921	2.7161	-0.775	-0.2135	3.00830	-0.4836	0.0785
11	-0.0910	0	0.4524	0.45244	0.09106	0.54350	0.5435
12	-0.5319	0.0232	-1.069	-0.3516	1.35521	-0.5372	0.1803
Mean	-0.0011	0.1711	-0.878	-0.2946	0.17234	-0.8776	-0.293
S.D.	0.69597	1.3031	1.5698	0.60781	1.45664	1.33492	0.6983
S.E.	0.20091	0.3761	0.4531	0.17546	0.42049	0.38536	0.2015
t	-0.0058	0.4550	-1.939	-1.6792	0.40985	-2.2775	-1.455

(1) The imbalance baseline rate ratio ($\log_e$ of a rate ratio$_{Icon/Placebo}$ is quite different from 0.000) may be taken into account by subtracting a $\log_e$(rate ratio$_{Icon/Placebo}$) value before from the $\log_e$ value after the intervention within the same pair. The average of the differences reflects the unbiased effect of the lambda-cyhalothrin impregnation programme. The paired t-test method is used for statistical analysis and was analysed in the same way as described in a).

(2) Critical $t_{10,0.05}$ value for degree of freedom of 11 is 2.201.
Critical $t_{10,0.01}$ value for degree of freedom of 11 is 2.718.

Annex 2.9 Summary of age- and sex-adjusted prevalence rate ratios.

a) Natural logarithmic values of the age- and sex-adjusted rate ratios (Icon/placebo) and their statistics.

Pair No.	Mass blood survey Oct-Nov'90 before dipping	Oct-Nov'91 after dipping	Differences (after - before)
01	-1.24605	-2.07201	-0.82595
02	0.639660	-2.94723	-3.58689
03	-4.44780	-2.14959	2.298207
04	-0.49950	-2.62183	-2.12233
05	0	-1.77469	-1.77469
06	0	0	0
07	2.912881	-1.76376	-4.67664
08	-3.29400	3.017973	6.311980
09	-0.49207	-2.33644	-1.84437
11	-4.52384	-4.76502	-0.24118
12	-2.30653	-0.79344	1.513088
Mean[1]	-1.20520	-1.65509	-0.44989
S.D.	2.161212	1.870924	2.887569
S.E.[2]	0.651630	0.564105	0.870636
t [3]	-1.84952	-2.93402	-0.51673
Converted[4] rate ratio		**0.191073**	**0.637697**
p value	<0.10	<0.02	>0.10

(1) - The imbalance baseline rate ratio ($\log_e$ of a rate ratio$_{Icon/Placebo}$ is quite different from 0.000) may be taken into account by subtracting a $\log_e$(rate ratio$_{Icon/Placebo}$) value before from the $\log_e$ value after the intervention within the same pair. The average of the differences reflects the unbiased effect of the lambda-cyhalothrin impregnation programme. The paired t-test method is used for statistical analysis.

(2) - SE = sd./√n , n = 11

(3) - Critical $t_{2m\,.\,0.10}$ value for degree of freedom of 10 is 1.813.
Critical $t_{2m\,.\,0.05}$ value for degree of freedom of 10 is 2.228.
Critical $t_{2m\,.\,0.02}$ value for degree of freedom of 10 is 2.764.

(4) - Converted rate ratio = e^{mean}

b) Analysis of prevalence rate ratio by age and sex.

MALE

	0-14 year			15+ year		
	Before	After	Diff	Before	After	Diff
Pairno	Lnrr(I/P)	Lnrr(I/P)	Aft-Bef.	Lnrr(I/P)	Lnrr(I/P)	Aft-Bef.
01	-2.61434	-2.57984	0.034494	-0.89843	-2.71366	-1.81522
02	0	-2.90369	-2.90369	0	-3.23436	-3.23436
03	-5.23909	-5.99396	-0.75486	-3.75341	0	3.753417
04	-3.12408	0	3.124087	-2.62615	-2.90369	-0.27753
05	0	0	0	0	-2.76094	-2.76094
06	0	0	0	0	0	0
07	0	0	0	0	0	0
08	0	0	0	-3.79500	4.091399	7.886399
09	4.520799	0	-4.52079	-4.21459	0	4.214593
11	-5.37196	-5.56167	-0.18971	0	-4.96882	-4.96882
12	-5.81213	-4.52079	1.291338	-5.73234	-0.90615	4.826191
Mean	-1.60371	-1.95999	-0.35628	-1.91090	-1.21784	0.693063
S.D.	2.997402	2.337967	1.895142	2.059336	2.331887	3.792335
S.E.	0.903752	0.704924	0.571407	0.620914	0.703091	1.143433
t	-1.77450	-2.78043	-0.62352	-3.07756	-1.73212	0.606125

FEMALE

	0-14 year			15+ year		
Summary	Before	After	Diff	Before	After	Diff
Pairno	Lnrr(I/P)	Lnrr(I/P)	Aft-Bef.	Lnrr(I/P)	Lnrr(I/P)	Aft-Bef.
01	-2.95396	0	2.953962	-3.03504	0	3.035048
02	-2.81090	0	2.810907	3.025671	-3.10353	-6.12920
03	-4.35572	-4.83628	-0.48055	-4.24800	-0.50102	3.746980
04	0	0	0	2.782013	-3.14510	-5.92712
05	0	0	0	0	0	0
06	0	0	0	0	0	0
07	4.615120	-3.41482	-8.02995	0	0	0
08	0	0	0	-3.67532	0	3.675326
09	3.931825	0	-3.93182	-4.28260	-3.41482	0.867771
11	-5.65848	-4.83628	0.822204	0	0	0
12	-0.32504	0	0.325041	-1.57438	3.282452	4.856833
Mean	-0.68701	-1.18976	-0.50274	-1.00069	-0.62564	0.375057
S.D.	3.004394	1.974137	2.935654	2.476495	1.856304	3.467405
S.E.	0.905860	0.595225	0.885134	0.746692	0.559697	1.045463
t	-0.75841	-1.99884	-0.56798	-1.34017	-1.11781	0.358747

c) Age-adjusted sex-specific prevalence rate ratio

	MALE			FEMALE		
	Before	After	Diff	Before	After	Diff
Pairno	Lnrr(I/P)	Lnrr(I/P)	Aft-Bef.	Lnrr(I/P)	Lnrr(I/P)	Aft-Bef.
01	-0.98266	-2.66732	-1.68465	-3.00656	0	3.006561
02	0	-3.12699	-3.12699	0.713188	-2.70952	-2.70952
03	-4.57681	-4.98110	-0.40429	-4.28819	-1.16313	3.125060
04	-2.84233	-2.48549	0.356841	2.369113	-2.75017	-5.11928
05	0	-2.34736	-2.34736	0	0	0
06	0	0	0	0	0	0
07	0	0	0	3.612532	-2.40045	-6.01298
08	-3.33997	3.652049	6.992028	-3.24229	0	3.242294
09	-0.19974	0	0.199740	-0.89712	-3.01472	-2.11760
11	-4.39614	-5.22546	-0.82931	-4.64466	-3.77551	0.869147
12	-5.76293	-1.58249	4.180445	-0.93401	2.884716	3.818727
Mean	-2.00914	-1.70583	0.303312	-0.93800	-1.17534	-0.17251
S.D.	2.117486	2.422067	2.771564	2.534919	1.870558	3.282426
S.E.	0.638447	0.730281	0.835659	0.764308	0.563995	0.989690
t	-3.14692	-2.33585	0.362962	-1.22725	-2.08396	-0.17430

d) Mass blood survey coverage.

BEFORE	ICOB			Placebo			Total		
Pairno	Total	Exam.	%cover	Total	Exam.	%cover	Total	Exam.	%cover
01	182	112	61.5	419	330	78.8	601	442	73.5
02	255	165	64.7	445	278	62.5	700	443	63.3
03	93	60	64.5	115	82	71.3	208	142	68.3
04	273	202	74.0	472	271	57.4	745	473	63.5
05	86	51	59.3	704	266	37.8	790	317	40.1
06	221	163	73.8	102	62	60.8	323	225	69.7
07	59	56	94.9	207	146	70.5	266	202	75.9
08	66	40	60.6	95	85	89.5	161	125	77.6
09	110	97	88.2	114	50	43.9	224	147	65.6
11	44	22	50.0	57	37	64.9	101	59	58.4
12	159	128	80.5	69	52	75.4	228	180	78.9
Total	1548	1096	70.8	2799	1659	59.3	4347	2755	63.4

AFTER	ICOB			Placebo			Total		
Pairno	Total	Exam.	%cover	Total	Exam.	%cover	Total	Exam.	%cover
01	193	145	75.1	427	276	64.6	620	421	67.9
02	259	200	77.2	440	200	45.5	699	400	57.2
03	100	77	77.0	118	45	38.1	218	122	56.0
04	263	218	82.9	451	201	44.6	714	419	58.7
05	88	71	80.7	714	460	64.4	802	531	66.2
06	228	184	80.7	88	85	96.6	316	269	85.1
07	51	40	78.4	215	143	66.5	266	183	68.8
08	63	57	90.5	96	86	91.5	157	143	91.1
09	108	135	125.0	102	122	119.6	210	257	122.4
11	39	32	82.1	55	61	110.9	94	93	98.9
12	170	141	82.9	81	52	64.2	251	193	76.9
Total	1562	1300	83.2	2785	1731	62.2	4347	3031	69.7

f) Age- and sex-adjusted prevalence rates and natural logarithmic transformed values.

MASS BLOOD SURVEY

Summary	BEFORE DIPPING				AFTER DIPPING			
	ICON		Placebo		ICON		Placebo	
Pairno	Std	Lnstd	Std	Lnstd	Std	Lnstd	Std	Lnstd
01	0.952291	0.669003	3.558412	1.516974	0	0	0.694083	0.527141
02	0.605303	0.473312	0.272027	0.240612	0	0	1.805320	1.031517
03	0	0	8.443884	2.245367	1.270837	0.820148	11.66366	2.538736
04	0.467734	0.383720	0.835576	0.607358	0	0	1.276101	0.822464
05	0	0	0	0	0	0	0.489847	0.398673
06	0	0	0	0	0	0	0	0
07	1.740976	1.008314	0	0	0	0	0.483638	0.394362
08	0	0	2.595062	1.279561	1.944981	1.080102	0	0
09	2.628836	1.288911	4.363562	1.679628	0	0	0.934439	0.659817
11	0	0	9.118895	2.314404	0	0	11.63340	2.536344
12	2.078792	1.124537	21.77418	3.125627	1.462966	0.901366	3.355731	1.471492
Mean	0.770357	0.449800	4.632873	1.182684	0.425344	0.254692	2.939639	0.943686
S.D.	0.915881	0.480140	6.264469	1.043069	0.710195	0.419759	4.202792	0.853639
S.E.	0.276148	0.144768	1.888811	0.314497	0.214132	0.126562	1.267191	0.257382
e^{mean}		1.567998		3.263123		1.290064		2.569436
$e^{mean}-1$		0.567998		2.263123		0.290064		1.569436

Annex 2.10 Log$_e$ rate ratio$_{Icon/placebo}$ by aqueous dilution factor.

a) On malaria incidence

Aqueous dilution factor of 5% EC Icon®	Average standardised rate ratio Before adjusted 1:100	1:200	1:300	After adjusted[1] 1:100	1:200	1:300
Number of pairs	3	5	4	3	5	4
12 months before the impregnation						
Mean standardised rate for:						
Lambda-cyhalothrin	64.17	42.60	81.87			
Placebo	69.88	61.30	48.55			
Mean log$_e$ rate ratio	-0.083	-0.357	0.506	1.000	1.000	1.000
(s.d.)	(0.632)	(0.649)	(0.740)			
8 months after the 1st impregnation						
Mean standardised rate for:						
Lambda-cyhalothrin	5.05	12.75	32.08			
Placebo	16.90	7.67	14.60			
Mean log$_e$ rate ratio	-1.086	0.461	0.752	-1.000	1.000	0.250
(s.d.)	(1.224)	(1.331)	(1.122)	(1.732)	(1.225)	(1.500)
8 months after the 2nd impregnation						
Mean standardised rate for:						
Lambda-cyhalothrin	2.67	10.17	14.04			
Placebo	19.61	15.20	35.16			
Mean log$_e$ rate ratio	-1.725	-0.371	-0.878	-1.667	0.200	-1.750
(s.d.)	(1.658)	(2.238)	(0.449)	(1.155)	(1.924)	(0.500)
Summary of 16 months after impregnations						
Mean standardised rate for:						
Lambda-cyhalothrin	13.94	37.98	48.90			
Placebo	36.68	42.42	51.72			
Mean log$_e$ rate ratio	-0.924*	-0.109	-0.055	-0.667	0.200	-0.750**
(s.d.)	(0.260)	(0.511)	(0.636)	(0.577)	(0.447)	(0.957)

1 - The rate ratios were adjusted by taking into account the prior rate ratio.

* - Significantly different from 1.00, p value < 0.05

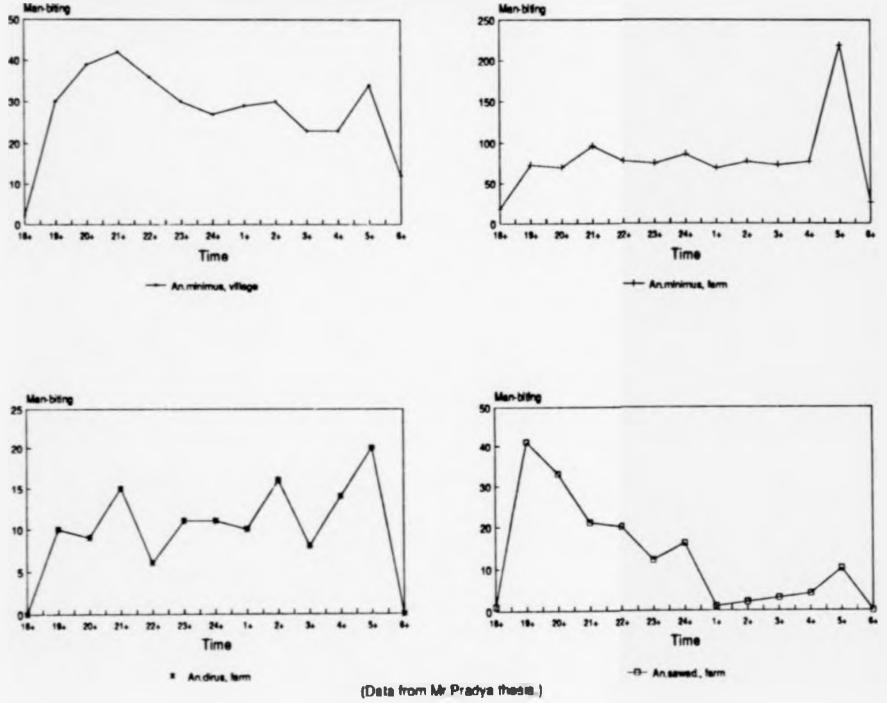
** - Significantly different from 1.00, p value < 0.01

b) On malaria prevalence

Aqueous dilution factor of 5% EC Icon[R]	Average standardised rate ratio Before adjusted 1:100	1:200	1:300	After adjusted[1] 1:100	1:200	1:300
Number of pairs	3	4	4	3	5	4
Oct-Nov'90 before the impregnation						
Mean $\log_e$ rate ratio	-0.331	-3.066	0.000	1.000	1.000	1.000
(s.d.)	(0.286)	(2.120)	(2.292)			
Oct-Nov'91 after the impregnation						
Mean $\log_e$ rate ratio	-2.244*	-0.974	-1.894*	-1.914**	2.092	-1.894
(s.d.)	(0.431)	(3.298)	(0.889)	(0.184)	(3.037)	(2.790)

1 - The rate ratios were adjusted by taking into account the prior rate ratio.
* - Significantly different from 1.00, p value < 0.05
** - Significantly different from 1.00, p value < 0.01

Annex 2.11 Biting time of potential vectors.



(Data from Mr Pradya thesis.)

Annex 2.12 Map of the 24 study bans.