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# Malaria control in Papua New Guinea results in complex epidemiological changes

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## SUMMARY

**With a renewed interest in large-scale malaria interventions, knowledge about the possible long-term effects of such interventions on the nature of malaria transmission is essential. We document complex changes in malaria epidemiology over the last 40 years associated with changing malaria control activities in Karimui, an isolated area in Papua New Guinea. An initially equal distribution of *Plasmodium falciparum*, *P. vivax* and *P. malariae* changed to currently 68% *P. falciparum*, after passing through a phase of transitory *P. vivax* dominance, when control started to fail. Initial drops in malaria prevalence proved difficult to sustain and present post-control levels are significantly higher than pre-control levels. The example of Karimui indicates that unsustained control can lead to changes in malaria patterns that may leave a population worse off.**

## Introduction

Renewed awareness of the immense human and economic costs of malaria has brought malaria control once again to prominence on the international public health agenda. There has been extensive discussion of the possible effects of malaria interventions on protective immunity and patterns of morbidity (1,2), but less attention has been given to the long-term effects on malaria transmission itself, especially in areas outside Africa that have complex malaria patterns.

In Africa a massive resurgence of malaria was seen after cessation of control in many areas (3) but the absence of significant levels of non-falciparum malaria preclude investigation of differential control effects on individual malarial species. Following the cessation of DDT spraying in Sri Lanka in 1964, *Plasmodium vivax* quickly re-established itself causing major epidemics (4). Control was reintroduced and, following the switch from vector control to exclusive treatment of malaria cases and the first reports of chloroquine resistance, a steep rise in *P. falciparum* cases was observed (4), although *P. vivax* remained the dominant parasite (5). In areas of Asia and South America with ongoing malaria control programs, for instance Thailand and Brazil, a shift from *P. falciparum* to *P. vivax* preponderance occurred in the last 20 years (6,7) despite rising levels of drug-resistant *P. falciparum*. The contrary trend of *P. falciparum* replacing *P. vivax* was, however, observed in parts of India with high levels of drug and insecticide resistance (8). These patterns indicate complex relationships between control activities and the transmission of different malaria species in different parts of the world.

In Papua New Guinea (PNG), where all 4 human *Plasmodium* species and a multitude of vectors occur, the malaria control program

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that lasted from 1960 to the early 1980s was associated with a notable shift from *P. vivax* to *P. falciparum* predominance (9,10). In Karimui, an isolated area without road access, located approximately 1000 m above sea level (settlement range c 900-1200 m) to the south of the main highland cordillera, control started later and lasted longer than elsewhere in PNG. Good, detailed malariological data from pre-control (1965) (11), early into control (1971) (12), breakdown of control (1981) (13) and current, post-control times (2001-2002) (14) are available from a series of large malaria surveys in this area. Further, the history of control is relatively well documented (14). This offers an exceptional opportunity to investigate changes in malaria epidemiology in relation to malaria control activities.

## Materials and Methods

This paper used results from four major malaria surveys, conducted between 1965 and 2002, in the Karimui and Daribi area on the Karimui Plateau, South Simbu. These surveys published in reports or scientific papers contained detailed descriptions of sample locations and populations and presented data in ways that allowed collating samples that were comparable in areas and age groups covered. A number of other malaria surveys, in particular from the control period, could not be used for this comparison as they lacked sufficient detail and/or documentation. Most were only available from field research notes from one author (RH) and either only covered parts of the Karimui area or did not contain sufficient detail on populations covered. The comparison was thus restricted to the 4 published surveys.

Following an initial malaria mass blood survey of the Karimui area in 1962, a major pre-control survey was conducted in August 1965 by the Malaria Control Service and included 3937 people in both Karimui and Daribi census districts (CD) (11). Control measures began in early 1968, and included indoor residual spraying (IRS) with DDT (indoor residual spraying , two spray rounds annually) and mass drug administration (chloroquine and pyrimethamine, administered during the spray rounds from 1968 to 1970 only) (Figure 1). Regular mass blood surveys were carried out twice a year to assess control efficacy, and a scientific assessment of the malaria situation under control was conducted in October-November 1971 (12). The 1971 study assessed 978 people on the Karimui Plateau.

A decade later, following reports of high levels of child malnutrition, in-depth epidemiological surveys were carried out in Karimui during August-September 1981 by members of the Simbu Land Use Project, the Provincial Department of Health and the PNG Institute of Medical Research (IMR). The aim of these surveys was to determine the prevalence of malnutrition, malaria and intestinal parasites (13). Malarial infections and spleen rates were assessed in a total of 1591 individuals from 7 villages in Karimui and Daribi CD. Twice-yearly spraying was continued until 1978, when control was scaled back. Spraying continued at irregular intervals and decreasing coverage until the early 1980s (15) (Figure 1). The 1981 survey thus coincided with the period of failing control characterized by erratic interventions and decreasing coverage and effectiveness.

In 1984 vector control was officially abandoned and until 2002 treatment of all presumptive malaria cases with chloroquine and primaquine has been the mainstay of malaria control throughout PNG. Although insecticide-treated bednets have become increasingly available in PNG in recent years they are virtually absent in Karimui villages. As part of a larger study into the epidemiology of malaria throughout the PNG highlands, 765 individuals in 4 villages were examined for malarial infections and morbidity between July 2001 and May 2002 (14). In addition, a further 263 individuals were surveyed in December 2002 in 3 additional villages surrounding Karimui Station as part of an ongoing study on molecular markers of drug resistance. For the present analysis, results from the latter study were included with those from the wider 2001-2002 survey.

Although the same villages were not included in each of the four main studies used here, all of the studies conducted cross-sectional community surveys across the same areas of the Karimui Plateau, and comprised all age groups in similar proportions. As original data were only available from the 2001-2002 surveys, age categories were set to provide maximum correspondence between tabulations in the published studies. The data from the most recent surveys were then reanalyzed to fit

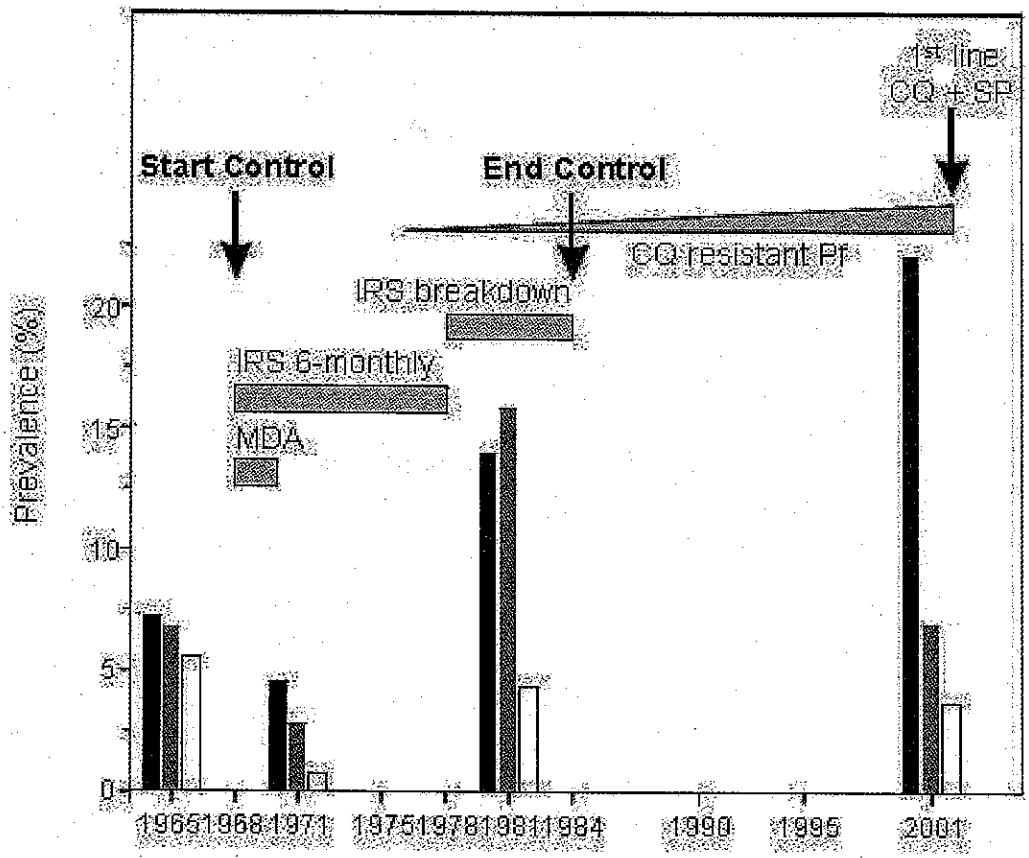


Figure 1. Changing prevalence of malarial infection in relation to control interventions in Karimui, 1965-2002.
*P. falciparum* = black bars; *P. vivax* = grey bars; *P. malariae* = open bars.
IRS = indoor residual spraying with DDT; MDA = mass drug administration; CQ = chloroquine; SP = sulfadoxine-pyrimethamine.

these categories. All comparisons between and within studies were done using chi-squared tests and logistical regression.

## Results

The first detailed survey in 1965, prior to control measures, found a malaria prevalence rate (PR) of 19.4% across Karimui, with similar amounts of *P. falciparum*, *P. vivax* and *P. malariae* present (Table 1 and Figure 1). After malaria control started in 1968, overall malaria levels were rapidly brought down to 7.1% by 1971, with *P. falciparum* dominating over *P. vivax* (PR: 4.5% vs 2.8%, p = 0.05) (Figure 1). *P. malariae* was permanently reduced. The age distribution of cases was little affected during the early phase of control, with parasite prevalence peaking at 1-4 years both in 1965 and 1971 (Figure 2).

The faltering of the control program in the late 1970s and early 1980s resulted in a massive surge in malaria transmission. In 1981 overall prevalence had climbed to over 30%, significantly exceeding pre-control levels (Table 1) ($p < 0.001$). The increase was strongest in *P. vivax* (PR: Pf 13.9%, Pv 15.8%, Pm 4.4%) (Figure 1) and peak prevalence shifted to the 5-9 year (Pv) and 10-14 year (Pf, Pm) age groups (Figure 2).

By 2001, some 20 years after the breakdown of control, the overall prevalence of malaria had not risen significantly ($p > 0.5$). However, there has been a major shift in species composition (Table 1). While the overall prevalence of *P. vivax* decreased to pre-control levels (6.9%) the prevalence of *P. falciparum* increased to 22.1% and now accounts for 68% of infections. Peak prevalence of parasitaemia has shifted back towards younger age groups in *P. vivax* and *P. malariae* infections, but not in *P. falciparum* (Figure 2).

In the 2001-2002 surveys there is a highly significant difference both in overall

**TABLE 1**

MALARIA PREVALENCE RATES, SPECIES COMPOSITION AND SPLEEN RATES IN KARIMUI, 1965-2002

| Year | N | PR (%) | Species composition | | | SR (%) |
|---|---|---|---|---|---|---|
| | | | Pf % | Pv % | Pm % | |
| 1965 | 3937 | 764 (19.4) | 36.7 | 34.6 | 28.7 | - |
| 1971 | 978[a] | 69 (7.1) | 56.2 | 34.3 | 9.6 | 262 (24.2) |
| 1981 | 1591 | 482 (30.3) | 40.7 | 46.4 | 12.9 | 488 (30.7) |
| 2001-2002 | 1028 | 314 (30.5) | 68.4 | 21.1 | 10.5 | 400 (38.9) |

[a]Sample size for spleen rate 1084
N = number of people tested
PR = number of people positive for malaria and prevalence rate (%)
Pf = *Plasmodium falciparum*
Pv = *Plasmodium vivax*
Pm = *Plasmodium malariae*
SR = number of people with an enlarged spleen and spleen rate (%)

prevalence and age distribution of cases in relation to the distance of the surveyed village to a health centre. In villages within 1 hour's walk of Karimui and Negabo health centres, overall prevalence was 22.4% compared to 35.6% in those further away ($p < 0.001$) (Table 2) and age of peak prevalence was significantly higher ($\chi^2 = 12.6$, df = 3, $p = 0.006$). Such differences were not observed ($p > 0.2$) in the 1981 surveys, with overall prevalence of 33.6% and 36.0% in the 1-9 year and 24.0% and 20.2% in the over 15 year age groups in villages within or beyond 1 hour's walking distance from the nearest health centre, respectively.

## Discussion

The data from Karimui not only show that the impressive initial reductions in malaria transmission achieved by control measures were difficult to sustain, but that the epidemiology of malaria in the area has been significantly changed over the course of these interventions.

The slight shift to *P. falciparum* early during the control period was probably due to mass drug administration, as has been seen in other parts of the country (9). Surprisingly, the roles were reversed when the control efforts were breaking down. Between 1971 and 1981, irregular spraying and cessation of mass drug administration favoured *P. vivax* transmission. Several factors may have contributed to this change: its long-lasting liver stages, short extrinsic cycle and faster production of gametocytes (16) make *P. vivax* easier to transmit in marginal or fluctuating circumstances. Additionally, prolonged DDT spraying elsewhere in PNG led to a shift in vectors towards early- and outdoor-biting mosquitoes (17). Early-biting mosquitoes in PNG tend to be younger and more likely to carry *P. vivax* sporozoites (18), thus favouring transmission of *P. vivax*.

The resurgence of malaria following collapse of regular control was very rapid. Mass blood surveys in the same areas conducted by the malaria control services (usually at the time of spraying activities) in the 6-18 months preceding the 1981 survey, found a significantly lower overall prevalence (14-15%) with a similar predominance of *P. vivax* as in the 1981 survey (R. Hide, personal communication).

As elsewhere in PNG, *P. falciparum* became the dominant malaria species in Karimui after the complete cessation of vector control in the 1980s, while *P. vivax* fell back to pre-control levels (Figure 1) with a comparable age distribution (Figure 2). Indiscriminate use of 4-aminoquinolines in

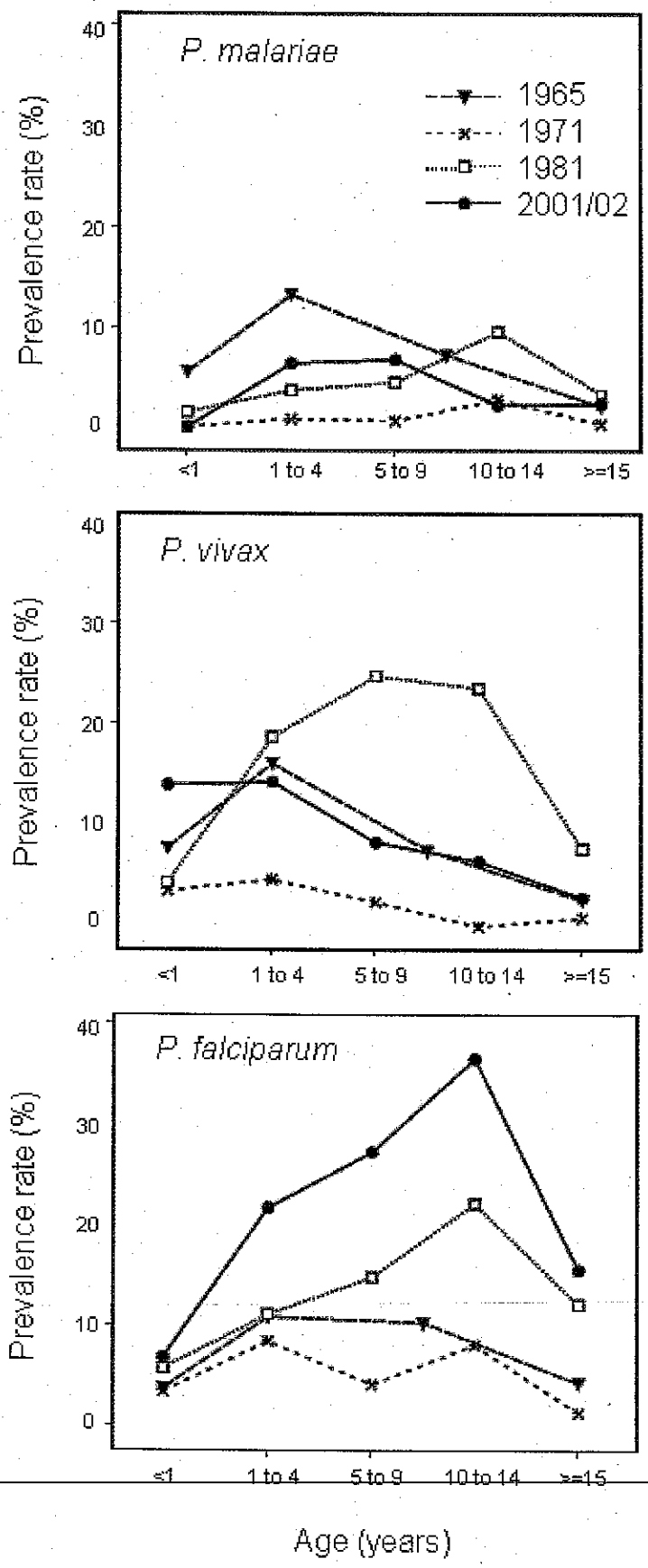


Figure 2. Age-specific prevalence of different malarial infections in Karimui, 1965-2002.
Data from 1965 survey did not allow differentiating into 5-9 year and 10-14 year age groups and data are thus given for 5-14 year age group only.

**TABLE 2**

AGE-SPECIFIC PREVALENCE OF ALL MALARIA INFECTION IN 2001-2002 SURVEYS IN RELATION TO DISTANCE FROM NEAREST HEALTH CENTRE

| Age | Within 1 hour's walk | | >1 hour's walk | |
|---|---|---|---|---|
| | No | % positive | No | % positive |
| <1 year | 8 | 0.0 | 57 | 36.8 |
| 1-4 years | 50 | 18.0 | 84 | 57.1 |
| 5-9 years | 75 | 33.3 | 101 | 50.5 |
| 5-15 years | 57 | 35.1 | 119 | 46.2 |
| >15 years | 153 | 15.0 | 324 | 21.3 |
| **Total** | 343 | 22.4 | 685 | 35.6 |

combination with poor compliance and the advent of resistant *P. falciparum* (9) are the likely reasons for this shift. Both result in poor clearance of infections and increased gametocyte production, thus fuelling *P. falciparum* transmission. Ongoing in vivo follow-up and studies of molecular drug resistance markers show high levels of 4-aminoquinoline resistance in Karimui (J. Marfurt and I. Mueller, unpublished data). *P. malariae,* with the longest extrinsic cycle and still full susceptibility to 4-aminoquinolines, never fully recovered.

During the period that these changes in malaria epidemiology occurred, other significant changes in human-environment relations took place in the Karimui area that may have influenced malaria transmission. Most importantly, these included a substantial population increase (a doubling between 1962 and 1990), and a shift in settlement pattern from dispersed longhouses to centralized nucleated villages. These trends resulted in larger, more clustered areas of cultivation and human use. Such conditions favour vectors such as *Anopheles punctulatus* that breed in open, sunlit pools (17) that result from agriculture and other human activity, thus increasing the chance of transmission.

It has been argued that a change to a sedentary, agricultural lifestyle favoured the transmission of *P. falciparum* over *P. vivax* and contributed to the worldwide *P. falciparum* dominance (19,20). It cannot be ruled out, therefore, that changes in population density, agriculture and settlement pattern at Karimui may have contributed to the dramatic shift towards *P. falciparum* following the collapse of control activities. It may also have helped to seal the fate of *P. malariae,* a parasite well adapted to endemicity in sparse and mobile human populations (19).

Malaria control may also have affected immune status causing shifts in the age of peak prevalence. Early on, age-distribution was little affected, but during the breakdown of control there was a clear shift towards older children, as shown by the 1981 survey. In the 20 years since cessation of vector control, peak prevalence of malarial infections has shifted back to younger age groups except in areas with ready access to antimalarial drug treatment. This indicates that 13 years of control, even if imperfectly done, reduced immunity in children. Similar shifts in distribution of malaria cases to older age groups with decreasing transmission were also seen in Africa where they were linked to increases in bednet coverage and changes in first-line treatment (2).

This Karimui example demonstrates that, as elsewhere in areas with complex malaria patterns (4-9), major control interventions not only result in temporary reductions in levels

of transmission but may be associated also with significant, unpredictable and possibly long-term shifts in malaria epidemiology. Such shifts might be especially marked if control is not properly maintained and, as in the case of Karimui and PNG in general, may leave an area worse off than before control. While the Karimui experience does not contraindicate renewed malaria control efforts, it highlights the importance of monitoring changes in malaria epidemiology, as well as the need to sustain successful interventions once started.

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