

## COMMUNITY-BASED PROGRAM FOR MALARIA CASE MANAGEMENT IN THE BRAZILIAN AMAZON

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**Abstract.** In areas of drug-resistant malaria, control programs may restrict chemotherapy until malaria has been confirmed via microscopy to contain costs and toxicity. In Brazil, patients travel to centralized laboratory posts (FNS) at great cost for diagnosis and treatment. A program was established through the bars of a mining town offering free dipstick diagnosis and mefloquine treatment on a 24-hr basis; falciparum malaria dipstick tests are accurate and easy to use. Outcomes were compared with historical data and results of a neighboring non-intervention village. Guidelines for dipstick use and treatment were followed for 98% of visits. The number of FNS visits was reduced from 2,316 (expected) to 1,097 (observed) with 626 dipstick tests applied. Ninety-five percent of those who visited the FNS experienced onset of malaria symptoms in the town where the FNS was located. There was an unexpected doubling of the malaria hospital admission rate. We demonstrate that dipstick testing can be used in a sustainable, community-based program that should be applicable in a wide variety of settings.

### INTRODUCTION

Ideally, malaria treatment should be initiated during the early stages of illness at the peripheral community level to minimize morbidity and mortality. In these settings, clinical diagnosis is usually all that is available; because this diagnosis is so inaccurate, there is a tendency to be cautious, which leads to overdiagnosis and overtreatment. Another reason for overtreatment may be the financial incentives of drug vendors to sell antimalarial drugs. This overtreatment may be reinforced in the majority of cases because patients have self-limiting, nonmalaria illnesses that improve after (but not due to) antimalarial therapy.

When cheap and safe drugs, such as chloroquine, were still effective, this may have been the preferred method of patient management. However, we have now learned that even with such attractive characteristics, limiting a drug's use should be considered in order to delay the development of resistance. The majority of malarious areas outside of Africa are now chloroquine resistant; effective, alternate regimens are expensive and sometimes toxic. For these reasons, many have recommended restricting chemotherapy to microscopically diagnosed cases. In this scenario, the feasibility of microscopy is the limiting factor determining the extent to which case management will be available in the periphery.

Brazil's malaria is largely restricted to the Amazon region where the vivax to falciparum ratio is ~ 2:1, with variations depending on the specific locale.<sup>1,2</sup> Falciparum malaria is resistant to chloroquine, and Fansidar (pyrimethamine + sulfadoxine), with quinine + tetracycline or mefloquine<sup>3,4</sup> are effective alternatives. The malaria control program is largely dependent on centralized government laboratory posts (FNS) that provide microscopic diagnosis and treatment at no cost to patients. In areas where microscopy was unavailable, an attempt was made to continue with clinical diagnosis and therapy with chloroquine, but these efforts were quickly abandoned when patients experienced a high number of falciparum malaria treatment failures. Despite the large number of FNS laboratories, such facilities are still far from large segments of target populations, and patients spend much time and money traveling to them. This scenario in Brazil is typical of many countries where governments are trying

to restrict antimalarial use to microscopically confirmed cases.

Recognizing the need for laboratory diagnosis at the village level, Ettling and others<sup>5,6</sup> evaluated the use of mobile clinics for microscopy and treatment on a semiweekly basis. Although this method did reach otherwise neglected groups (women and children), half of the subjects requesting slides were not ill, and ~ 84% did not have symptoms that would have led to central clinic visits. As might be expected, the slide positivity rate fell from ~ 20% in the central clinics to 5% at the mobile clinics. Along these lines, other studies to improve peripheral management resulted in no reduction in the number of visits to central clinics.<sup>7</sup> Clearly, the diagnostic arm of peripheral programs is vulnerable to gross overuse and abuse. But it is not clear if making services more accessible in place and time will worsen or improve this problem.

An antigen-detecting dipstick test (ParaSight-F, Becton Dickinson, Franklin Lakes, NJ) has been shown to be accurate in symptomatic patients for falciparum diagnosis when used by minimally trained personnel.<sup>8–10</sup> The specificity and sensitivity for detecting falciparum malaria in a Brazilian clinic was 97 and 91%, respectively.<sup>11</sup> Regarding effective therapy, a hospital-based study in the same area in 1995–1996 showed a mefloquine cure rate of 99% in 94 subjects.<sup>4</sup>

Our objective was to set up and evaluate a community-based program in the Brazilian Amazon for malaria management that used dipstick diagnosis and mefloquine treatment. Once the program was introduced, our intent was to interfere as little as possible in the operational aspects except to monitor results and ensure that supplies were always available to health care providers. An economic analysis of this project will be presented elsewhere.

### MATERIALS AND METHODS

**Study design.** The results of the intervention, applied to Baixão (the test village) for 1 year, were compared with data from Baixão from the previous year (historical control). In addition, a similar, nearby village (Mutum) was designated as a concurrent control and monitored during the 2 years to

assess the year-to-year variation in outcome variables. The principal outcome was Baixão's change in the number of patient visits to the FNS laboratory and the number of hospitalizations of patients with malaria. Besides this, we examined the number of dipstick diagnoses performed, adherence to indications for dipstick test use, the proportion with positive results, and the reasons why some patients continued to use the FNS system.

**Site and population.** The study was conducted in Apiacas municipality (population ~ 7,800), a gold-mining area of Brazil's southern Amazon. The rural areas surrounding Apiacas are divided in 2 major mining villages, Baixão and Mutum. The Apiacas hospital serves all the surrounding mining villages (including Baixão and Mutum). There are no paved roads, and dirt roads are often impassable during the 5-month rainy season. The climate is tropical and humid, with marked wet and dry seasons. Malaria is by far the greatest cause of morbidity and hospital admissions. A government-sponsored FNS clinic (providing microscopy) and a 32-bed hospital is located in Apiacas. Diagnosis and treatment at the Apiacas FNS clinic is provided at no cost to patients. Private pharmacists are also available, but their services are seldom used because of the high costs. First- and second-line falciparum malaria treatment are composed of a 7-day regimen of quinine plus tetracycline, and mefloquine (1,000-mg single dose), respectively. For many years, falciparum malaria has been highly resistant to chloroquine and Fansidar.

Baixão is an isolated gold-mining area with ~ 2-km radius and a population of 750, the majority of which are adult migrant workers whose history of malaria exposure and immunity varies widely. Baixão is 32 km from the town of Apiacas, whose FNS clinic performs nearly all of the malaria diagnosis (microscopic evaluation) and treatment for Baixão's patients. A population-based cross-sectional survey at the start of the study showed that ~ 5% of the Baixão population had asymptomatic *Plasmodium falciparum* parasitemia (carriage). Power is limited to a few portable generators and gas operated mining sluices. Although the trip between Baixão and Apiacas takes only a few hours in the dry season, transportation is difficult to arrange, especially during the rainy season and at night. The average time for arranging and round trip travel to Apiacas is estimated to be 1.5 days and costs an average of US\$40. Miners earn an average of US\$10 per day.

Mutum, the adjacent mining village with malaria ecological factors very similar to Baixão's, is located 35 km from Apiacas in the other direction. There is very little interchange between the 2 villages regarding malaria management. Mutum itself has an FNS malaria clinic (with microscopy services) located within the village, but patients also go to Apiacas to visit the FNS clinic and hospital. Otherwise, conditions are similar to those of Baixão.

**Intervention.** Six of Baixão's 15 bars were chosen to perform malaria diagnosis and treatment. Locations were selected to ensure that all inhabitants would be within a 20-min walk from a participating bar. In addition, bars needed to have enough staff members (2–3 people) so that 24-hr service 7 days a week was possible. Each bar's staff participated in a 2-day training session that covered malaria epidemiology, biology, clinical aspects, indications for diag-

nostic tests, and procedures for treatment and referral. It is noteworthy that only 2 hr were needed to adequately train personnel specifically on the use and interpretation of dipsticks. We instructed providers to do the following:

1. Refer all subjects with severe symptoms (including vomiting) to Apiacas hospital regardless of malaria diagnostic test results.

2. Perform dipstick diagnosis on those presenting with at least one of the following: fever, headache, backache, generalized myalgia, or a history of one of these symptoms within the past day. We discouraged, but permitted (as long as symptoms were recorded), dipstick tests on anyone not fulfilling the symptom criteria.

3. Repeat any initially negative dipstick within 12–24 hr at the patients' request. If the second result was still negative, they were to refer the patient to Apiacas for persistent or worsening symptoms.

4. Record the number who presented but did not meet criteria for dipstick test use. For those getting a dipstick test, record the patient's, name, age, sex, presenting symptoms, test result, and treatment or referral. Keep all dipsticks for collection and reexamination by FNS staff.

5. Prescribe chloroquine treatment for dipstick-negative cases of malaria. Observe mefloquine treatment (1,000-mg single dose) for dipstick-positive cases. And redose if vomiting occurred within an hour.

6. Work voluntarily, without compensation from patients or the government.

7. Educate those in their respective village areas about all aspects of the program. Periodic population-based interviews would be conducted by the study investigators to assess the level of community education.

Ethical approval was obtained from the National Health Program, and subjects gave oral informed consent to participate.

**Monitoring.** At the Apiacas and Mutum FNS clinics, data routinely collected were not affected by the study. Data collected included patients' demographic data, residence, site of acquisition of malaria, results of microscopic diagnosis, and treatment administered. During the intervention, all patients who lived in Baixão and who presented to the Apiacas FNS were asked their reason for the visit and if they had previously sought diagnosis and treatment through Baixão's bars. At the 30-bed Apiacas hospital, admission criteria and recording of data were not affected by the study, with illness diagnosed as malaria only when there was smear confirmation. Near the beginning of the second year, there was a change in hospital staff that may have affected admission criteria and rates. The FNS staff of Apiacas was instructed to visit the staff of the 6 participating bars on a monthly basis to ensure that records were being kept, to replenish dipstick and mefloquine supplies, and to collect dipstick tests.

In Baixão, the population's acceptance of our intervention was evaluated through 2 cross-sectional surveys (randomly selecting households for interviews) during the second month and at the end of the intervention. During both interviews, patients were asked about knowledge and use of the new program as well as hospitalizations for malaria during the previous year. During the second interview, subjects

TABLE 1  
Observed FNS visits (% with falciparum malaria)\*

Program	Baixão (n = 750)	Mutum (n = 900)
First year (old program)	3,306 (15.6%)	5,005 (16.2%)
Second year (new program)	1,097 (7.5%)	3,507 (13.1%)
DS	626 (19.8%)	

\* FNS, central laboratory clinic; DS, dipstick tests applied. By calculation, the expected Baixão second-year visits were 2,316. The following results were significant ( $>0$ ) at  $P < 0.0001$ : (1) the number of FNS visits from Baixão (1,097) continuing during the second year; (2) the number of dipstick tests applied (626); (3) the reduction in the number of observed Baixão visits to Apiacas FNS compared with expected numbers during the second year ( $1,219 = 2,316$  [expected] -  $1,097$  [observed], a 53% reduction); and (4) the number of reduced visits not accounted for by dipsticks [ $593 = 2,316 - (1,097 + 626)$ ].

were also asked about their willingness to pay for dipstick tests.

**Data collection and analysis.** The principal outcomes were the number of Apiacas FNS visits and malaria hospitalizations from Baixão during the study intervention. By use of historical data from the year immediately preceding our study intervention (yr1) and adjustments for the year-to-year variation (on the basis of Mutum's data for the 2 study years), we calculated the expected (exp) number of visits that would have occurred from Baixão under the old program for the second year (yr2). This was compared with the observed (obs) number of visits from Baixão during the second year:

$$\text{Baixão}_{\text{exp yr2}} = \text{Baixão}_{\text{obs yr1}} \times (\text{Mutum}_{\text{obs yr2}} / \text{Mutum}_{\text{obs yr1}})$$

The same method (observed versus expected) was used to study the change in hospitalizations from Baixão, where the year-to-year adjustment was based on Mutum's hospitalization rates (from examination of hospital records), and the Baixão rates were based on community-based cross-sectional interviews. The number of malaria deaths ( $\sim 1$  per year) from Baixão was considered too low to monitor as an outcome.

A multiplier effect was defined as the number of FNS visits prevented (expected minus observed) divided by the number of dipstick tests applied. One would expect one dipstick test to prevent one visit, resulting in a multiplier effect of 1. This multiplier effect can also represent overuse when the ratio is much less than 1. For example, in the results of Ettling and others<sup>6</sup> cited above, the multiplier effect of mobile clinic diagnosis would be 16%. For our study, the multiplier effect was also calculated by month to see if there was a trend with duration of the program (learning curve) or if there was a correlation with dipstick positivity ratio. Statistical conclusions were based on chi-square tests, confidence intervals of incidence density ratios, and confidence intervals of the difference of these ratios.

## RESULTS

In general, the new system was easily implemented, easily sustained, and well received by the inhabitants of Baixão. The quality of record-keeping and information obtained by the participating bars of Baixão, the cross-sectional interviews, and the Apiacas and Mutum FNS clinics were complete and meticulous. Volunteers were easily taught to use

TABLE 2  
Observed malaria hospital admissions\*

Program	Baixão (n = 750), by interviews of community sample	Mutum (n = 900), by sample of hospital records
First year (old program)	11 admissions, 75 person-years	33
Second year (new program)	50 admissions, 196 person-years	27

\* On the basis of the sample, the expected number of Baixão malaria hospital admissions for the second year was 90 (see Methods). The calculated observed number of hospitalizations during the second year was 191, over twice the number expected ( $P = 0.026$ , incidence density comparison for  $H_0$  (the null hypothesis): identified first year/identified second year = 33/27).

and accurately read the dipstick tests. The hospital records were adequate regarding the number of patients, admissions, and diagnosis, but the patients' place of residence was often not detailed enough. The populations of the 2 mines remained constant throughout the study period, and no new malaria control interventions were initiated. The number of FNS clinic visits, the number of dipstick tests used, and the dipstick test results are given in Table 1 for Baixão and Mutum.

Of the 1,097 patients who continued to use the Apiacas FNS clinic during the second study year, 1,042 (95%) reported that they did so because symptoms began in Apiacas. In Baixão, all patients presenting for diagnosis had symptoms that met the criteria for use of dipstick tests. Only 9 patients with initial negative dipstick tests findings returned for a second dipstick test after 24 hr because of continuing symptoms.

The overall multiplier effect was  $1,219 \div 626, \sim 2$ , significantly greater than 1 ( $P < 0.0001$ ), implying that 2 visits were prevented for each dipstick test applied. There was no correlation by month of the multiplier effect with study duration, but there was a significant inverse correlation with the proportion of dipstick tests that were positive ( $P < 0.005$ ; data not shown). Table 2, shows Baixão's and Mutum's malaria hospitalization rates for the years before and during the dipstick intervention. For Mutum, the results are based on a sample of hospital records and the ratio between years are intended to be used as an adjustor for the year-to-year variation in rates that would have occurred in Baixão without intervention. For Baixão, results are based on community interviews and are intended to reflect the total number of patients admitted with malaria. We observed about twice the rate of malaria hospitalizations from Baixão during the year of intervention compared with the expected rate (on the basis of Baixão's first year and Mutum's adjustment for year-to-year variation).

There were 75 and 196 villagers in the 2 cross-sectional surveys, which were performed in July 1996 (3 months after the start of dipstick test intervention) and August 1997 (6 weeks after the end of the intervention), respectively. In the first interview, 85% knew of the new program, and 32% had already used it. In the second interview, 87% knew about the system and 65% had already used it. Of those who had not used dipstick tests, only 12% ( $\sim 30$  people) did not trust this diagnostic method. This number is compatible with the 55 visits (at 2 visits per resident) by those who used the

Apiacas FNS clinic even though their symptoms began in Baixão. In the second survey, many who denied the knowledge of the system had recently arrived to work in the mines. Of those who had used dipstick tests, 98% said they were satisfied with the system and would use it again instead of going to the Apiacas FNS. The average amount users were willing to pay for the dipstick was US\$5.60 (we did not ask about willingness to pay for mefloquine). Almost all the participants considered this new program a great advantage for the community. The program still continues (and has begun in neighboring communities), although the study officially closed in the summer of 1997.

#### DISCUSSION

This project represents an effort to establish a new strategy for malaria control in the Amazon, targeting those who had the poorest access to diagnosis and treatment. There are many such areas in the Amazon, typically gold-mining and agricultural areas, with populations too small or malaria attack rates too low to warrant a government clinic with microscopy services. These are also the remote frontier areas where population migration makes establishing and maintaining such clinics very difficult. Compared with the existing program and literature reports of attempts to extend to the community other strategies for malaria case management, our program was an unprecedented success. In general terms, success was measured by the frequent, appropriate use of the new system and a corresponding reduction in reliance on the old.

This project's design is really that of an ecological study with the intent to look at individual behavior, rather than ecological effects. There is an inherent danger in concluding that the changes in behavior we observed were caused by our intervention because there could be confounding variables present during our intervention but not in our historical or concurrent controls.<sup>12</sup> The most obvious confounder is a difference in malaria transmission or a difference in the incidence of other diseases that cause malaria like symptoms.

Despite these shortcomings, our study can be used to describe the way in which dipstick tests were used by this community-based program. A significant ( $> 0$ ) number were used with a high proportion positive. There was little change in this pattern over a 1-year period. A significant number continued to use the old system because of convenience, with only a small fraction not trusting the results of dipstick tests. Interviews indicated that the community coverage (i.e., awareness and use) of the intervention was high. Despite the intervention, there continued to be a significant ( $> 0$ ) number of malaria hospitalizations. A more definitive study would have required a large number of villages randomized to intervention and control groups in an attempt to adjust for confounding effects. These descriptive results can be viewed as a pilot effort to describe the use of dipstick tests in such communities.

For the reasons cited above, further analysis comparing observed results to expected outcomes are questionable and prone to confounding effects. However, with this caveat, if one considers the calculated number of expected clinic visits and hospital malaria admissions, there was a reduction in the number of clinic visits, with about half of these patients not

being assessed by a dipstick test. The number of hospital malaria admission doubled. All of these results are statistically significant. It is possible that these observations are related through the following mechanism. When diagnosis and treatment are reliable and easily accessed, a significant number of patients who would normally have traveled to central clinics would delay diagnosis at the community level. Those with nonmalaria illness ( $\sim 70\%$ ) would experience spontaneous cure, whereas those with malaria become sufficiently ill because of this delay to require hospitalization. The high number without malaria who spontaneously cure without diagnosis contributes to our observed multiplier effect and high dipstick test positivity rate, whereas those with malaria (say 30%) may be the reason for the increase in malaria hospitalizations.

Regarding this point, for malaria cases diagnosed in Baixão during the second year, we expected  $\sim 120$  more malaria cases than observed, which is a number similar to the increased number of malaria hospitalizations (100) from Baixão. Unfortunately, our study of hospitalized patients was not detailed enough to determine the exact reasons for the increase—only that it did occur and should be monitored closely in future studies.

We did not feel it necessary to compare dipstick tests to microscopy during our study because studies have shown that the majority of errors result from specific laboratory workers who misread tests.<sup>8-10</sup> These types of errors can be avoided by careful training and, as in our study, periodic collection and reexamination and confirmation of readings themselves. On the basis of the results of a recent study in a similar population of the same area,<sup>11</sup> we expect, compared with microscopy, our positive predictive value and negative predictive value to be 90 and 97%, respectively. We consider the “over-treatment” of the 10% of patients with false-positive findings to be negligible compared to the treatment of patients with asymptomatic parasitemia (related to the carriage rate of 5% of the *entire* population). To minimize the effects of the 3% false-negative (one minus the negative predictive value) results, providers were trained to repeat negative tests within 24 hr for patients who remained symptomatic.

There are 2 main reasons to consider our study only a pilot study. First, as mentioned above, a larger number of randomized villages needs to be studied comparing dipstick tests and existing program for malaria management. Second, we are uncertain exactly how the new program changes behavior and how each change is related to outcome. For example, for the number of FNS visits prevented, one could stratify the results into those seeking diagnosis via dipstick test and those who do not. In both groups, there are other levels of stratification based on the presence or absence of falciparum malaria infection and having a correct or incorrect diagnosis. How much each of these contributes to the outcomes of visits prevented and excess hospitalizations has yet to be determined.

Furthermore, beyond stratification of the study by subpopulations, the underlying cause of each effect is still not clear. For example, although it is tempting to think that those with falciparum malaria who are diagnosed and treated in the periphery are benefiting from early diagnosis and treatment, they may actually be worse off if they waited longer

(than under the old program) before seeking diagnosis for reasons described above. Are these the types of patients contributing to higher malaria hospitalization rates, or is it another group for another reason? These underlying reasons need to be identified in future studies to see if and how the program can be improved.

There are effects that we have not attempted to measure that others may consider important. This program may have affected transmission, duration of patient suffering, and appropriate antimalaria drug use, leading to a slower development of resistance. Health authorities in multidrug-resistant areas may find some of these reasons compelling arguments for program implementation. Worldwide, many community settings exist that are similar to ours, but there are also many areas with equally important but different outcome variables. For example, in such communities, it may be more important to reduce mortality or the indiscriminate use of antimalarial drugs by the private sector. However, we do feel that following the principles used in our program would give the best results (whatever the outcomes) in almost all situations. Easy access to effective diagnosis and treatment, community education and responsibility, and periodic government monitoring should apply to all malaria control programs. If these criteria are not established and sustained, the private sector will quickly fill and capitalize on this new niche.

**Acknowledgments:** We thank Dr. Elisabeth Duarte for her helpful insights and comments regarding outcomes. We thank Edson Pertile, Gemercindo Lopes, David Manuel de Santana, and the health staff of Apiacas municipality for their help in conducting the field work. We thank Dr. Kathleen Pang for critical review.

**Financial support:** This project received funding from the Tropical Diseases Research Unit of the World Health Organization, Geneva, and the National Health Foundation (FNS), Brazil.

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