

Home treatments alone or mixed with modern treatments for malaria in Finkolo AC, South Mali: reported use, outcomes and changes over 10 years

Bertrand Graz^{a,*}, Merlin Willcox^b, Diafara Berthé^c, Denis-Luc Ardiet^a, Jacques Falquet^a,
Drissa Diallo^d and Sergio Giani^e

^aCommunity Health Association, Geneva, Switzerland; ^bNuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK; ^cField survey team, Sikasso, Mali; ^dDepartment of Traditional Medicine (DMT), Bamako, Mali; ^eAid to Development of Traditional Medicines (AIDEMET), Bamako, Mali

*Corresponding author: Tel: +41 21 314 6946; E-mail address: bertrand.graz@chuv.ch

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Background: In 2003, a study in Mali showed that 87% of episodes of uncomplicated malaria were first treated at home. We investigated whether treatment-seeking patterns in Mali had changed 10 years later.

Methods: In 2013, we repeated the retrospective treatment-outcome study on 400 children with presumed malaria in the same area.

Results: Most children with reported uncomplicated malaria were still first treated at home (76% [196/258] in 2013 vs 85% in 2003; $p=0.006$), rather than in modern health centres (20% [52/258] in 2013 vs 12% in 2003; $p=0.01$). Overall, 58% of children with uncomplicated malaria were treated with herbal medicine alone, a significant increase from 24% 10 years earlier ($p<0.001$). This was associated with an increase in use of *Argemone mexicana* decoction from 8% to 26% ($p<0.001$), with a reported cure or improvement in 100% of cases among those aged >5 years. For severe malaria, first treatment was sought less often from a traditional healer compared with 10 years earlier (4% vs 32%; $p<0.001$) and more often from a modern health centre (29% vs 17%; $p=0.04$).

Conclusions: Two trends that emerged are that there is a greater use of modern health facilities for treatment of severe malaria, and a greater use of traditional medicine alone for treatment of uncomplicated malaria.

Keywords: Malaria, Natural products, *Plasmodium*, Rural health, Traditional medicines, Treatment-seeking

Introduction

In 2003, we surveyed the treatments used against malaria and the associated outcomes in two rural Malian populations with limited access to modern healthcare (Bandiagara and Sikasso districts).¹ This ‘retrospective treatment-outcome’ (RTO) study found that 87% of uncomplicated episodes of malaria were first treated at home with either traditional or modern medicines, or a combination of both. Clinical recovery was more than 98% with any type of treatment. For presumed severe malaria, the overall case fatality rate was 17%: it was not correlated with the type of treatment used. This survey was followed by several research and development projects that took place over the subsequent 10 years, especially in the Sikasso district of Mali.

First, an in-depth analysis of the RTO study data was done to identify the traditional treatments associated with the best outcomes. This was identified as the *Argemone mexicana* (AM) decoction, which was then studied in a dose-escalating clinical trial in 2004,² and in a randomised controlled trial in 2006.³ This

process called ‘reverse pharmacology’ or ‘bedside-to-bench’⁴ showed that AM’s safety and clinical effectiveness in the home management of presumed uncomplicated malaria were similar to those of artesunate-amodiaquine.⁵ Although this local preparation has not yet been the subject of widespread recommendations by public health authorities, results of the study were presented to the study population during community feedback sessions held by the research team in surveyed villages, and open to the whole population. Such feedback was part of the ethical rules agreed upon for the research project.

Second, a close collaboration was established with the regional hospital in Sikasso in 2006 to improve the quality of care for children with severe malaria. Before the intervention, the case fatality rate of severe malaria in Sikasso hospital was around 24%. After the quality improvement intervention, the case fatality was 17%.^{6,7}

In 2007, artesunate-amodiaquine and artemether-lumefantrine were adopted as the first-line treatments for malaria, and a policy was adopted to make them free of charge for children <5 years of age in government hospitals, community health centres and in

some areas where village health workers were trained. There were, however, frequent problems with supplies. Rapid diagnostic tests (RDTs) have also become free of charge for children attending government health centres, and where RDTs are available, Mali has adopted the WHO policy of testing before offering treatment. From August 2011, a confidential enquiry into maternal and child deaths was initiated in the same community, with regular feedback to the community of key health education messages, such as rapid treatment-seeking for severe malaria.

The question raised, 10 years after the first RTO study in the area was: 'What is the treatment-seeking behaviour for children with presumed malaria, in an endemic area of sub-Saharan Africa?' We also investigated reported patient outcomes as they were seen as a potential key factor to explaining health-seeking behaviour.

Methods

Study description

Due to the war in the north of the country, it was not possible to return to the area of Kendié (Bandiagara district). As a result, we had to limit this new survey to the area of Finkolo AC (Sikasso district, southern Mali).

We used the same method of RTO study as in our previous survey conducted in 2003¹ in order to make comparisons possible. We asked the same questions on the care of children (0 to 17 year-olds), with the same definitions of cases, treatments and providers. Any fever was considered to be uncomplicated malaria unless another cause was identified. Severe malaria was 'any fever with coma or convulsions during (or shortly after) the rainy season'; this category may include febrile seizures related to other causes than malaria parasites in the blood. The use of clinical symptoms alone to define malaria is relevant in the south of Mali because the detection of *Plasmodium* in the blood is poorly correlated with the disease itself in high-endemicity areas where there are many asymptomatic carriers.⁸ This survey cannot provide an estimate of incidence because only one malaria case per household (the most recent) was recorded, whatever the total number of malaria cases in the considered period. It should also be noted that this study cannot, due to the method used, provide any proof of treatment effectiveness or causal link with mortality and new symptoms.

The sampling method used was the same as a decade earlier,¹ based on the same population census. In order to produce a representative sample, all villages and neighbourhoods were visited and every person had an equal chance to be seen. The sampling unit was the family compound. In each compound visited, the latest case of malaria was selected for study, provided that it occurred within the past 3 months (for uncomplicated cases, the recall period was longer than in the first study because the rainy season was ending at the time of this survey) or during the past rainy season (for severe cases).

The questionnaire was pre-tested in 12 households to ensure that it was still relevant. Data were collected during January–February 2013.

Analysis

Data were entered with EpiInfo 7 (Atlanta, GA, USA) and analysed with EpiInfo 7, SPSS Statistics 21 (IBM, Armonk, NY, USA) and Stata 12 (StataCorp, College Station, TX, USA) softwares using the χ^2 and Fisher's exact statistical tests. For 2003–2013 comparisons, two

independent samples were drawn from the same population, 10 years apart. The 2003 data from the same subdistrict (Finkolo AC) of Sikasso district were used for comparison, although the total 2003 sample had turned out to be very homogeneous between districts.

Ethical approval

This questionnaire survey received ethical approval from the Ethics Committee of Mali's National Institute for Public Health Research.

Results

In 2013, in the Sikasso district, this new survey was very well accepted by the population: in the 514 households visited, no respondent refused to answer. A recent case of malaria in a child was described in 400 households (mean age 6 years; quartiles 25% <3 years, 75% <8 years; 202 girls, 198 boys). The classification based on usual local terms for uncomplicated and severe malaria is in close agreement with the classification based on definitions used in local health centres: 248 (96.1%) of 258 uncomplicated malaria were named locally as 'sumaya', 138 (97.1%) of 142 cases of severe malaria were named 'kôno'. The local diagnosis of sumaya is sometimes associated with other words (7% of sumaya cases [18/258]), the most frequent being 'djolidessé' (3% of the sumaya cases [8/258]), which means 'lack of blood' and corresponds to the signs of anaemia in modern medicine.

Figure 1 shows where first-line treatments were sought. For uncomplicated malaria, self-medication (treatment at home or by a relative who is not a traditional health practitioner or health professional) still represents the majority of first treatments (196/258; 75.9%), but significantly decreased from 85% in 2003 ($p=0.006$). Patients were brought to modern healthcare facilities

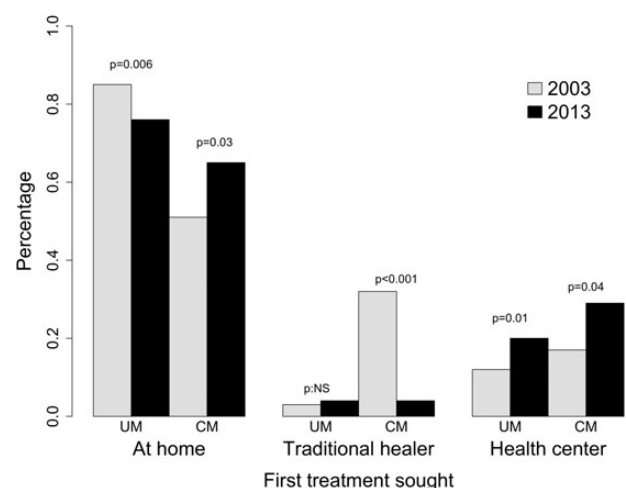


Figure 1. Proportion (%) of patients seeking their first treatment for uncomplicated (UM) and severe/complicated (CM) malaria, 10 years apart (2003 and 2013), at home, at a traditional healer or at a health centre.

in 20.1% (52/258) of uncomplicated malaria cases and 28.8% (41/142) of severe malaria cases, compared with 12% and 17%, respectively, in 2003 ($p=0.01$ and 0.04). A traditional practitioner was rarely consulted: in 10/258 and 6/142 cases of uncomplicated and severe malaria, respectively (i.e., 4% of cases of both types of malaria). This was a significant decrease for severe malaria (4% vs 32%; $p<0.001$).

Second-line treatments (119 cases) were sought more often in the modern healthcare system: 73% (43/59) of severe malaria cases (compared to 35% in 2003) and 63% (38/60) of uncomplicated malaria cases (compared to 26% in 2003). A traditional practitioner was consulted in less than 4% of second treatments for both kinds of malaria (compared to 20 and 30% in 2003) and a village health worker in less than 1% of cases.

In all locations, types of treatment were divided into three large groups: traditional, modern and mixed (Table 1). Compared with the 2003 figures, the proportion of patients treated for uncomplicated malaria with traditional medicine only had more than doubled. This significant increased reliance on traditional medicine is for a large part attributable to the increase in the use of AM. For severe malaria cases treated in a modern health centre, 28% of patients also received herbal medicines. Unlike 10 years earlier, there was no statistical association between the type of treatment used and distance to the modern health centre or possession of a motor vehicle.

The cost of treatment (in West African francs [CFA fr] where 1000 CFA fr=approximately €1.5) varied greatly. Half of modern treatments were obtained for free, but costs went up to 89 000 CFA fr. For traditional treatments, three-quarters were free, but there were also extreme prices of up to 75 000 CFA fr.

The proportion of patients with uncomplicated malaria who reported that they had improved or were cured was 93% (70/75) with combined treatment, 83% (27/33) with modern treatment alone and 78% (117/150) with only a traditional treatment (combined vs traditional alone $p=0.02$). Although by definition there is no death caused by uncomplicated malaria, three children classified in this study as ‘uncomplicated malaria’ died after modern treatment alone, and one when traditional treatment was used alone or in combination (non-significant difference $p=0.1$). Two of these children had an anaemic syndrome (djolidesse) and received a blood transfusion (hence would be classified ‘severe’ in the hospital). Among the other two (both <1 year-old), one had a bulging fontanelle (possibly due to meningitis) and one had cough and vomiting (possibly

due to a respiratory infection). All but one of these first modern treatments followed by death were received in a health centre.

For severe malaria, the rates of reported cure or improvement after the first treatment were 71% (35/49) after a combined treatment, 74% (25/34) after a modern treatment and 47% (25/58) after a traditional treatment alone (modern vs traditional; $p=0.007$). However deaths from severe malaria (6%) were more frequent when modern treatment alone had been used (7/41 cases compared with 2/119 when traditional treatment [alone or in combination] was used; $p=0.001$). A second treatment was sought not only if the disease persisted or worsened (62.6%; 72/115), but also when the patient had improved after first treatment (33.9%; 39/115), or even was cured (1.7%; 2/115). No sequelae were reported in 2013, compared to 5% of severe episodes and 0.5% of simple episodes reported 10 years earlier.

Among local treatments, there was an increase in the reported use of AM in the 10 years, from 39 to 142 mentions as the first treatment used, i.e., 35% of patients have used it in 2013 (40% of uncomplicated malaria and 28% of severe malaria). Its use was combined with a modern treatment in 36% of cases. In the 68 cases where AM was used according to the same indication as in the randomised controlled trial in the same district, which compared AM with artesunate-amodiaquine for uncomplicated malaria, reported outcomes were better than with all other traditional medicines taken together (Figure 2; AM vs all others: 91% vs 71% cure or improvement; $p=0.006$). In the 34 children >5 years old who received AM, results were 100% cure or improvement, compared to 74% among those using other traditional treatments in the same age group. The need for second-line treatment has been considered an indicator of failure or success of the first-line treatment. After a traditional treatment alone with AM (71 cases), a second treatment was given to 8 of them (11%), same proportion as in the prospective randomised controlled trial. In this survey, AM, when used as second treatment, was followed by healing or improvement in all the cases.

Discussion

The objective of this study was to describe the changes in health-seeking behaviour for the care of children with presumed malaria, in an endemic area of sub-Saharan Africa during a 10 year period (2003–2013). We also investigated reported perceived patient

Table 1. Number and percentage of patients receiving each type of treatment in Sikasso district, Mali, in 2003 and 2013

Type of treatment	Uncomplicated malaria			Severe malaria		
	2003	2013	p-value	2003	2013	p-value
Modern only	106 (29.2%)	33 (12.7%)	<0.001	22 (21.1%)	6 (4.2%)	<0.001
Traditional only	87 (23.9%)	150 (58.1%)	<0.001	48 (46.1%)	82 (57.7%)	NS
Both	168 (46.2%)	75 (29%)	<0.001	34 (32.9%)	54 (38%)	NS
Total	363	258		104	142	

NS: not significant.

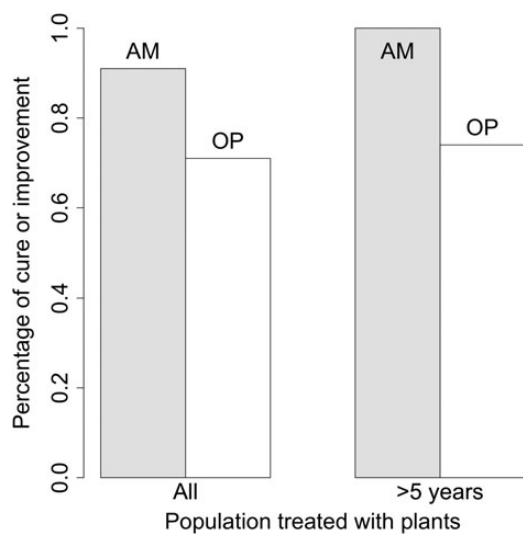


Figure 2. Proportion (%) of patients with presumptive uncomplicated malaria with reported improvement or cure, according to the traditional treatment used: *Argemone mexicana* (AM) versus all others plants (OP).

outcomes as they were seen as a potential factor explaining health-seeking behaviour.

Compared to 2003, in 2013, slightly fewer children with suspected uncomplicated malaria were treated at home, but self-medication still accounted for three-quarters of the first-line treatments. Traditional herbal preparations remained the most frequent treatment type (58% of first treatments), associated with relatively good reported clinical outcomes. Main trends appear as follows: more use of modern health facilities; less consultations with a traditional healer for severe malaria and more use of traditional medicine alone for uncomplicated malaria.

The changes in treatment seem to partly follow the official recommendations given to the population in Mali i.e., to use the modern health system.⁹ Such recommendations have often been made in the studied area; recently as part of the dissemination of results of a confidential enquiry into maternal and child deaths. Another important event in the region was the death of Tiémoko Bengaly, the traditional healer who participated in the clinical trials of AM. There has been no successor, and a lack of successors might in part explain the present low consultation of traditional healers.

We should refrain from any conclusions about relative effectiveness of various types of treatments used because the study was not designed to inform on this. It is of course tempting to estimate a treatment's effect on observed improvements, saying that 'if someone has been cured after using this treatment, then this treatment is effective' (most users and many practitioners do so). However, such a statement requires more thorough scrutiny, for two reasons: many malaria episodes in semi-immune patients improve over time even without any care; and there might be a 'placebo' effect, the stimulation of the patient's healing potential. The current gold-standard for evaluating a treatment, the randomised controlled clinical trial, is very different from the RTO study method used here, the latter eliciting statistical associations that can only be used to generate future research hypotheses.

An application of this reasoning is due to the observed association of modern treatment and reported mortality: this does not

imply a causal link. All but one deaths occurring after the first treatment occurred after modern treatment from a modern health centre. One may wonder whether the cases treated with modern medicine were more severe (although classified in the same category of uncomplicated or severe malaria cases) than cases treated with medicinal plants. This is not supported by available data: age and reported symptoms were similar. However, the questionnaire may not have been sensitive enough to pick up differences. One could also hypothesise that modern care is often perceived as of poor quality,¹⁰ so people may try to avoid it and prefer to use traditional medicine. Modern medicine could be thwarted by the problems of fake medicines on the market, overflow of Emergency Services, lack of blood for transfusion, sometimes insufficient competence of health workers, delays in treatment-seeking and difficult geographical and financial accessibility of health centres. It is also possible that some of the reported cases of malaria were actually other diseases, which may not be equally balanced between the various types of treatments. Informal accounts reported that patients treated in modern health centres currently receive traditional preparations brought by the family at the same time, with the inherent risks of drug interactions. However, the fact that second-line treatments are modern in most cases may suggest that modern treatment is now seen as a 'last resort', despite the public health messages to immediately seek modern treatment.

The use of a local treatment made with the plant *Argemone Mexicana* seems to have spread in 10 years, and this happened without any official recommendation. An explanation of the phenomenon could be the effect of the interest for this treatment from researchers of the University of Bamako and beyond, and of clinical studies of the preparation, which took place in this locality in 2004² and 2006.^{3,5} Reported outcomes are strikingly similar to those obtained during the randomised controlled trial. It is also possible that the use of AM has been in a process of expansion regardless of the research activity deployed in recent years and that we found a phenomenon that had its source elsewhere, for example in the population's experience of favourable clinical outcomes linked to the use of this plant.

Limitations of this study include the rather artificial and schematic categorisation of treatment pathways into first and second treatments. This does not reflect the very complex process of treatment seeking. Data may be incomplete or biased because they stem from memories accumulated during the last 3 months (uncomplicated cases) or the whole rainy season (severe cases). Ambiguities may also come from the controversial definitions of malaria: we were dealing with a region where diagnostic and therapeutic decisions are essentially clinical because the detection of the parasite in the blood does not help much in the diagnosis in a population with a high proportion of asymptomatic *Plasmodium* carriers.⁸ Also, the clinical definition of severe malaria did not include 'severe anaemia', and the questionnaire did not ask how many convulsions a patient had had, so it is possible that some patients with a single convulsion were incorrectly classified as having had severe malaria, and that patients who only had anaemia were misclassified as 'uncomplicated malaria'. Patients may tend to exaggerate the observed outcomes with traditional treatments if they have identified researchers interested in the topic. It should be remembered that an RTO study does not prove the effectiveness of a treatment. Finally, war and

security problems due to kidnappings of expatriates have severely limited the presence of a part of the research team.

Because of their potential health impact, traditional practices should be more broadly assessed: in Mali, the role of traditional medicines has strong political support, with an active Department of Traditional Medicine where, for example, a syrup of AM is being developed¹¹ (and will need to be tested through a randomised controlled trial), in addition to the traditional recipe with the same plant.

A public health study could measure the health impact of recommendations on the use of the AM as first-line treatment for home-based management of malaria (for adults and children >5 years in an area with high plasmodium endemicity), with standard imported treatments kept as second-line treatments. The study should also assess the potential of such a policy in delaying the appearance of parasites resistant to current standard drugs.

Conclusions

In the regions studied, self-medication and local traditional medicine remain the most frequent treatment for malaria. Patients seen in the modern healthcare system are, therefore, a small proportion of all patients, but have increased in number compared to 2003. The use of *A. mexicana* has spread, along with, but not necessarily caused by, a strong interest from national and international researchers, and without any official recommendation by public health authorities. The use of this plant to treat uncomplicated malaria was associated with reported outcomes similar to those observed in a previous randomised controlled trial.

It would be useful to verify if explicit synergies between modern and traditional systems could have a positive public health impact, and if therapeutic products such as the AM recipe could be useful in other areas with high malaria endemicity and semi-immune populations. To study this, the plant preparation could be used within a pilot trial with quality-controlled plant material, and outcomes compared in districts where the plant was used, compared to districts where it had not been used. Such a study could also be designed to investigate whether the use of a medicinal plant as first-line treatment may delay the emergence of resistance to other antimalarial treatments and as such, keep them effective in the fight against malaria.

Authors' disclaimer: Courses on the method used here, the retrospective treatment outcome study for traditional medicines, are organised in the frame of a European project on research capability strengthening in Africa called MUTHI. An Online course is available at this address: <http://globalhealthtrials.tghn.org/elearning/the-retrospective-treatment-outcome-study/> Contact: Dr. Merlin Willcox, Department of Primary Health Care, University of Oxford. E-mail: merlin.willcox@phc.ox.ac.uk.

Authors' contributions: BG coordinated the study, conducted the analysis and prepared the draft manuscript; MW helped organise the study, conducted the field study during war times and revised the draft manuscript; DB conducted the data collection and entry; DLA helped in

data analysis and preparation of the manuscript; JF, DD and SG helped with study preparation, organisation and report. All authors read and approved the final manuscript. BG is the guarantor of the paper.

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