Malaria treatment practice in sub-Saharan Africa

A critical look at the need for improved public health infrastructure

Approaches to Development 2008
David Tordrup, 20020554
"Every 30 seconds a child dies from malaria"
Acknowledgements

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1 Abstract

The burden of malaria continues to affect some of the world's poorest populations with significant morbidity and mortality to follow. Development of drug resistance in the malaria parasite during the past decades has forced most countries in sub-Saharan Africa (SSA) to change their first line treatment from the inexpensive chloroquine and sulfadoxine-pyrimethamine drugs to the 10-20 fold more expensive artemisinin combination therapies (ACT). Inexpensive antimalarial drugs have traditionally been used to treat all febrile illnesses in SSA with significant waste to follow, but such practice needs to be revised in the advent of more expensive ACTs. The ability to correctly diagnose malaria and differentiate it from other diseases relies on the use of diagnostic tools such as microscopy, which implicates technical infrastructure in proper clinical case management. This report examines the current state of such tools in SSA and asks whether improvements are needed to ensure cost-effective implementation of ACTs.
2 Introduction

Malaria is an infectious disease caused by the unicellular parasite *Plasmodium* which causes more than 500 million infections each year and over 1 million deaths, 90% of which are children in sub-Saharan Africa (SSA). On the African continent malaria accounts for 10% of the total disease burden, and nearly 25% of all childhood mortality[1][2]. The disease has spurred widespread attention in recent years, with UN recognizing the eradication of malaria, HIV/AIDS and other diseases as a Millennium Development goal[3], the World Health Organization (WHO) pioneering the Roll Back Malaria (RBM) initiative together with UNICEF, UNDP and the World Bank[4], and significant capital backing for malaria research and prevention provided by the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM)[5] and the Wellcome Trust[6].

The almost complete eradication of malaria from Europe and Northern America during the 1950s and 1960s diminished interest in the disease in the western world, and malaria slowly drifted into neglect. Attempts to eradicate malaria from the African continent were however inadequate and unsuccessful, and to this day malaria remains a significant determinant for morbidity and mortality[7].

An inexpensive antimalarial drug, chloroquine (CQ), has been readily available even to poor African households, and for many years has been the hallmark of malaria treatment. Shortly after its introduction though the efficacy of the drug started to decline and numerous reports stated that the *Plasmodium* parasites were developing resistance. In recent years such resistance has been known to cause high mortality rates in areas where chloroquine is still in use, in many cases causing dramatic increases in child mortality[8].

The spread of resistance to CQ and its equally inexpensive counterpart sulphadoxine-pyrimethamine (SP), has been cause for concern in recent decades, especially due to the lack of inexpensive alternatives. Recent research has identified the active ingredient from a traditional Chinese herb remedy, based on the bark of the *Artemesia Annua* tree, and the compound, artemisinin, has proved efficacious against malaria[9]. Artemisinin is currently recommended by WHO as first-line treatment in combination with a second unrelated antimalarial, a so-called Artemisinin Combination Therapy (ACT)[10]. ACTs have proved efficacious in numerous field trials and have a good safety profile, although the treatment cost is around 10-20 times that of CQ or SP. The high cost has caused widespread concern about the affordability of the drug in African countries, were public health budgets may already be overstretched and end users may not be able to pay for the drugs[8][11][12]. So far, GFATM has financed the implementation of ACTs as first-line drugs in most African countries[13][14], but the question remains whether such drug policies are sustainable in the long term.

This report examines recent and current antimalarial treatment practices from a provider and user perspective, including the widespread practice of treating all febrile patients with malaria drugs. The cost-effective implementation of ACTs requires selective treatment of only those patients who are parasitemic, emphasizing the need for integration of diagnostic
facilities in malaria case management. The aim is to clarify whether effective case management and thus cost-effective implementation of ACT policies can be achieved by increasing technical capacity of the formal health sector or whether optimizations within the current framework are a more viable approach.

3 Approach and limitations

Because of weak information systems and underreporting in many SSA countries there is a lack of reliable statistical data. This report is based on articles available from all major scientific journals (as indexed by http://scholar.google.com) as of June 2008, but due to the geographical spread of the studies examined it is difficult to draw conclusions for individual countries. The data presented here is thus intended to portray the trend in SSA in general, and studies in particular countries are assumed to be generalizable, although it is recognized that cultural and geographical factors can play a role in interpreting results.

The scientific literature is searched for studies describing the current technical capacity of SSA health services, including their ability to diagnose malaria using microscopy. The technical and infrastructural conditions are contrasted with the behaviour of clinical personnel and those seeking treatment based on mainly qualitative data from behavioural studies.

4 The cost-effectiveness of ACTs

Because the symptoms of malaria are generic (fever, joint pains, loss of appetite, headache) and vary from patient to patient it has been virtually impossible to develop a sound clinical algorithm with good sensitivity and specificity[15]. Therefore where laboratory facilities for microscopic diagnosis are not available, many cases of malaria are treated presumptively or based on a "hunch" of the clinician, causing a widespread over-diagnosis of malaria[16]. Additionally, presumptive treatment fails to treat the actual cause of the disease in patients with negative parasitemia, which may be as debilitating (or even lethal) as failing to treat a malarial infection[17]. As an example, in a low transmission setting in Uganda, researchers found that only 24.8% of those treated presumptively for malaria were parasitemic, while 75.2% were given antimalarials without cause. Similarly, only 27.5% of non-parasitemic patients were prescribed an antibiotic[18]. While the practice of presumptive treatment has been tolerated in an era of inexpensive drugs, this approach is not likely to be feasible after the implementation of ACTs.

ACT drug regimens are made available from WHO at a subsidized price of US$2.4 per adult dose in contrast to CQ and SP which cost US$0.11 and US$0.14 respectively[8]. The 20-fold cost increase however is offset by gains in efficacy. A cost-effectiveness analysis from Zambia in 2007 showed that of 55,509 patients receiving either Artemether-Lumefantrine (an ACT) or the outdated SP treatment, cure rates were 98.2% and 68.4% respectively. The average cost per case cured was thus US$8.57 for the ACT compared to US$10.65 for SP
(these costs included drugs, diagnostics, personnel and other expenses)[19]. Importantly, the only intervention in this study was the implementation of an ACT, no attempts were made to improve diagnostic skills of health workers, who often treated malaria presumptively. The average cost is therefore representative of the actual treatment setting, and may be improved even further if treatment is withheld from malaria-negative patients.

While the cost per case cured is lower for the ACT treatment, it should be noted that the total cost for ACT was around 25% higher than for SP (US$406,370 compared to US$343,743). This underlines the need for treating only malaria positive patients in order to keep health expenditures from rising.

The safety of withholding treatment from negatively diagnosed patients was recently demonstrated in a study of Ugandan children presenting at a public health clinic[20]. All febrile children were referred for microscopy, which had a sensitivity of 99.6%, and only positive cases were given antimalarial treatment. Of a total of 2359 children with febrile illnesses, which would normally be treated presumptively, only 751 antimalarial treatment courses were prescribed, saving 1608 courses (68%) over 18 months. There were no serious adverse effects of this procedure. Not only did all parasitemic children recover, febrile illnesses that were not due to malaria were able to be followed up and treated with antibiotics.

A similar study from a hospital in Malawi found that the proportion of antimalarial prescriptions could be lowered from 39.9% to 6.6% of all prescriptions by implementing microscopy for febrile patients, effectively saving 3% of the total annual drug budget for the hospital[21].

It is clear that significant savings can be made by the correct use of diagnostic facilities, and that such savings are safe provided the accuracy of microscopy is high. The ability to selectively provide treatment for those in need is likely to play a major role in the long term implementation of national ACT programmes, but rests on two assumptions: Reliable laboratory testing must be available for the majority of health clinics dealing with malaria cases, and the majority of malaria cases should be dealt with in these clinics. These assumptions will be probed in the following sections.

5 Quality and accessibility of laboratory facilities

While data on the African health infrastructure is scarce[22], the general consensus in the literature is that public health infrastructure is inadequate in most cases and that little has been invested in building laboratory capacity (human resources and technical equipment)[23][7][24].

A few studies however have given in-depth information. In Kenya, the first line of medical care for the majority of the population is peripheral health centres. These are managed by Clinical Officers, who have 3 years basic training in medicine and management and are assisted by Laboratory Technicians with a 2-year basic course, no physicians are present in these health centres. In some cases, lack of qualified physicians means Clinical Officers
are also in charge of district hospitals and perform all clinical tasks including emergency surgery[25].

Access to continued training is limited and there is a severe shortage of manuals and reference books. Many health centres do not have designated laboratory rooms or even access to electricity or running water. Medical engineers who operate at regional levels do not have the tools or spare parts to maintain equipment such as microscopes. Additionally, no quality assurance schemes are in place to monitor output of the laboratories[25]. Tanzania and Uganda suffer from the same shortages as Kenya and Uganda is further short of laboratory staff, causing 60-83% of laboratory work to be performed by unqualified workers[25][26]. Similarly in Ghana untrained personnel account for 74% of the technical staff in 205 laboratories studied[23].

Even worse off are countries with a recent history of civil war such as Angola, where hardly any public health infrastructure exists at all and those who are employed in the health sector are grossly underpaid. Similar problems are found in the Democratic Republic of Congo and Sierra Leone[25].

A study from 2000 evaluated the state of microscopes in district hospitals in Malawi. Only half of all microscopes were reported to be in good condition and in use, the rest were not in use and in need of repairs. Regular service and repair is a prerequisite for keeping microscopes operational[27], yet none of the microscopes had ever been serviced or repaired. More worryingly, there were reports of microscopes without focusing ability and with fungal growth on the lenses being used for malaria diagnostic procedures[28]. The use of substandard equipment is very likely to impact the quality of diagnosis in a negative direction, although so far no studies have addressed this question directly.

Another study from Malawi reported that potentially infectious samples were not handled in a safety cabinet, there were no facilities for sterilization of tools and clinical waste was buried in an insecure pit due to lack of proper handling schemes. Understaffing meant that less than required time was spent on analyzing samples, although surprisingly even under these conditions sensitivity of malaria microscopy was high (90%). The lack of basic laboratory equipment and safety measures however are still cause for concern[29].

These data imply that human resource capacity in SSA is generally poor, there is a lack of qualified staff resulting in the use of untrained workers, and the equipment available to technicians is generally run down and unserviced. Laboratories generally do not implement quality control schemes or provide further education for technicians, and routines for laboratory safety are virtually non-existent.

Examining data collected by WHO seems to indicate that health infrastructure is somewhat correlated with gross national income (GNI). The number of physicians per capita rises steadily with GNI/capita (fig. 5.1, left), while the number of laboratory health workers show a similar but less pronounced tendency (fig. 5.1, right). These numbers indicate that economy certainly impacts public health infrastructure, but that perhaps especially laboratory infrastructure is also influenced by other factors.
Figure 5.1: Scatterplot of physicians (left) or laboratory health workers (right) per 1,000 capita versus gross national income per capita[22]. Blue points represent all 46 SSA countries, black line is a linear regression.

The geographical access for potential patients is evaluated here by comparison of the total area of three countries divided by the total number of health facilities available. This is by no means a rigorous approach but for the lack of appropriate data will act as a proxy for the discussion. The data on health facilities and country sizes are extracted from a study by Carter et al. in 1997[25], all countries described are included here (table 5.1).

<table>
<thead>
<tr>
<th>Country</th>
<th>Size (square miles)</th>
<th>Total number of health facilities(^1)</th>
<th>Square miles per health facility</th>
<th>Average maximal distance (miles) to facility(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya</td>
<td>224,961</td>
<td>549</td>
<td>409</td>
<td>11,4</td>
</tr>
<tr>
<td>Tanzania</td>
<td>364,900</td>
<td>421</td>
<td>866</td>
<td>16,6</td>
</tr>
<tr>
<td>Uganda</td>
<td>90,076</td>
<td>239</td>
<td>376</td>
<td>10,9</td>
</tr>
</tbody>
</table>

Table 5.1: Geographical coverage of all health care facilities. \(^1\)National-, zonal-, provincial- and district hospitals and health centres. \(^2\)Assuming each facility services a circular area, this figure gives the radius of the circle, and thus the maximal distance from a point in the service area to the facility.

In the best case, where health facilities are distributed as evenly as possible and as close to the centre of their geographical coverage as possible, the average person will have to travel 10-15 miles to reach a facility. Combined with poor transport infrastructure and high costs this can be a major deterrent to seeking treatment within the formal health sector[30][31]. Accessibility also tends to disproportionately affect the poor, who are more likely to live in remote areas and more likely to delay treatment seeking due to transport cost[31].
5.1 Diagnosis and treatment practice

Apart from the availability of laboratory services a major factor to consider is how they are actually used. In cases were diagnostic facilities are not available overdiagnosis of malaria can be reasonably expected, but more surprisingly, when laboratory services are available they are often used sporadically or the results are essentially disregarded.

A study from Kenya in 2006 demonstrated that while the majority of microscopy confirmed cases were treated with antimalarials (96%), an overwhelming proportion of negative cases (79%) were also treated, even though the test was ordered and evaluated by the health worker[32]. The sensitivity of microscopy under these conditions was down to 69%. A number of similar studies are summarized in table 5.2 below:

<table>
<thead>
<tr>
<th>Country</th>
<th>Diagnosis type</th>
<th>Sensitivity</th>
<th>% of negatively diagnosed treated</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya</td>
<td>Microscopy</td>
<td>69%</td>
<td>79%</td>
<td>[32]</td>
</tr>
<tr>
<td>Zambia</td>
<td>Microscopy</td>
<td>88%</td>
<td>39%</td>
<td>[33]</td>
</tr>
<tr>
<td>Tanzania</td>
<td>RDT(^1)</td>
<td>95%</td>
<td>(58%, 63%, 30%)(^2)</td>
<td>[34]</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Microscopy</td>
<td>71%</td>
<td>(55%, 63%, 27%)(^2)</td>
<td>[34]</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Microscopy</td>
<td>50%</td>
<td>48%</td>
<td>[35]</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Microscopy</td>
<td>75%</td>
<td>No data</td>
<td>[17]</td>
</tr>
</tbody>
</table>

Table 5.2: Studies reviewing quality of diagnoses and percentage of non-parasitemic patients treated.\(^1\)RDT = Rapid Diagnostic Test, a quick and simple finger prick diagnostic method.\(^2\)Study was conducted over three transmission settings (very low, low-moderate and high).

The lack of adherence to diagnostic results could be explained by the low sensitivity causing lack of confidence in results. However, there does not seem to be any inverse correlation between sensitivity and % of negatively diagnosed treated, for instance a sensitivity of 95% still caused overtreatment in up to 63% of patients, and a low sensitivity of 50% caused overtreatment in 48%, which would probably have been much higher if lack of confidence in test results were the actual cause.

What the figures do show however is the poor quality of microscopy in many settings. Microscopy is generally considered the most sensitive method for diagnosis, but relies on qualified technicians and adequately maintained equipment. The low sensitivities shown in table 5.2 are likely a combination of a lack of both.

The apparent failure to act on laboratory results has implications for the cost-effectiveness of ACT drugs. Following up on the study from Kenya[32] it was shown that simply adhering to the diagnostic data without any improvements in microscopy would reduce the cost per 1000 patients from US$2154 to US$1254[36]. An economic model expanding on the results of the Tanzania study[34] also showed that the cost of treatment is a direct function of the response to diagnosis of healthcare workers, as shown in fig. 5.2, left panel[37].

This model also demonstrated that transmission rates had a significant impact, with even a full (100%) response rate in high transmission settings (fig 1, right panel) incurring
5.2 Perception of diagnosis

There are many potential reasons why diagnostic data is not obtained or disregarded by health workers including lack of availability, lack of confidence in results, cost etc. A recent study from Ghana set out to identify which perceptions of health workers could impact the decision to use diagnostics: Availability of malaria microscopy was perceived as adequate by 68% of all respondents, while 82% always or frequently believed in the accuracy of results. 95% said they frequently or always received results back from the laboratory and the same percentage stated they rarely or sometimes did not order tests because they were too expensive. Interestingly, 88% stated that they frequently or always used laboratory tests to
diagnose patients while 64% at the same time indicated they frequently or always diagnosed malaria without ordering microscopy. Accordingly only 44% of respondents answered that laboratory tests changed their management of patients[38].

The laboratories at the study hospital were found to be in good condition with most (80%) of staff well educated and 4/5 laboratories routinely performing quality control measures. Moreover malaria microscopy was available 7 days/week, 24 hours/day. The perception of health workers correlated well with this, except perhaps the lower than actual perception of the availability of malaria microscopy of 68%. But this does not explain why as many as 64% of respondents stated diagnosing malaria without laboratory tests, and only 44% regarded laboratory tests as important for case management.

The study indicates that even when high quality laboratory facilities are available and clinicians express confidence in their results, clinical judgement continues to take precedence over diagnostic tests, resulting in an overwhelming extent of false positive malaria diagnosis[38]. The impact of such behaviour on the fatality rate is non-negligible according to a study in Uganda, where incorrect antimalarial treatment of children with negative microscopy caused a 1.5-fold increase in fatality, probably due to failure to recognize the correct cause of the disease[39]. A similar study in Tanzania found that 66% of inpatients with presumed severe malaria but a negative microscopy slide were not given antibiotics, and here too case fatalities were 1.8-fold increased in microscopy negative patients[17].

Improving laboratory conditions as an isolated measure is therefore not likely to improve the adherence of health workers to diagnostic results nor stimulate the use of them, as argued above. If the perception of quality and availability of laboratory services is not the cause for their under use, more subtle reasons must abound. It has been suggested that the risk of not treating a patient with malaria is perceived as more important than the unjustified use of drugs[40], which would explain why many negative patients are treated with antimalarials, but does not explain why these same patients are not receiving antibiotics for their actual illness.

These observations indicate that effective case management may not be as much a question of technical capacity as it is a behavioural issue, and that interventions to improve the use of existing diagnostic facilities are likely to be more beneficial than programs to increase laboratory capacity.

6 Treatment outside formal health care sector

To address effective case management as a whole it is also necessary to consider those cases that never reach health clinics or hospitals. Estimates of the prevalence of self-treatment vary widely between countries (7-94%[41]) but it is commonly agreed that a significant proportion of all disease cases are treated at home[41][27][42] and it is estimated that half of all antimalarial drugs are sold outside the public sector[43]. The reasons for self-treatment are numerous but the most significant are distance from health clinics, perception of disease
severity and economical concerns[43]. Additionally public health clinics have been known to run out of drugs, have inconvenient opening hours and long waiting times or be staffed by personnel who are rude and in courteous[44][24] contributing to the reluctance of many people to use such facilities.

Self-treatment has been described by several researchers as just one step in a "hierarchy of resort". From the time symptoms start to appear to the disease is eventually cured, several courses of action may be taken. Often the initial response is self-treatment with antimalarials purchased from the informal sector (markets, street vendors, unlicensed shops), and in cases where symptoms persist further steps may involve visits to traditional healers or health centres[44]. A study from Burkina Faso showed that 55% of patients presenting at a health clinic with malaria already had chloroquine in their blood, only 20% of these had levels within the therapeutic range and alarmingly around half had potentially toxic levels[45]. These results confirm the notion of widespread self-medication, but also indicate that knowledge on correct dosage is severely limited.

As a step in the "hierarchy of resort" however, self-treatment has the advantage of being immediately available, which according to WHO may help reduce mortality from severe malaria[10]. Treatment outside the formal health care system may not be ideal, but as distance to health clinics has been negatively associated with their usage, the ability to acquire drugs locally means treatment can be (and mostly is) started within a few hours after symptoms begin[44]. Accordingly in a study from Togo 97% of home-based treatments were commenced within 24 hours, in contrast to those visiting health centres where only 17% of patients arrived within 24 hours[43].

The question of proper dosage is important to reduce cases of recrudescent infections and the development of resistance, and can be addressed from both the consumer and the supplier side. Because informal drug sellers have little or no relevant education they are unable to give appropriate guidelines for the drugs they sell[44], are willing to supply inappropriate drugs or to reduce the dosage for economic reasons[40]. Such improper advice is likely to be important since many people do not discriminate between informal sellers and licensed pharmacists[40].

On the other hand, the consumer may have his/her own perceptions about what dosages are sufficient, in most cases meaning that treatment is halted when symptoms clear. Leftover medication is often saved for family or friends to be used in the next bout of illness, especially in poorer communities[41]. The high rate of illiteracy in many poor regions exacerbates improper dosing practice as printed instructions provided with medications are useless in these cases[46]. Even in settings with higher literacy, instructions may be written in a foreign language or use incomprehensible technical terms, limiting their use in practice[24].

6.1 Perceptions of etiology and treatment

In settings where self-treatment is abundant local perceptions of disease etiology are important for the treatment seeking behaviour. While the biological route of infection from
mosquito to human with the consequent clinical manifestation of "malaria" is undisputed in the scientific community, local perceptions of not only transmission but of the actual concept of malaria may vary widely.

In a study in Nigeria, 44% of respondents identified "playing in the sun" as a cause of malaria. Drinking dirty water was also thought to be associated with the disease, and only 4% correctly associated mosquito bite with malaria[47].

The biomedical condition of malaria is mirrored in several local disease categories, for instance "asra" translates roughly to fever and diagnosis of asra corresponds with malaria infection among the Dangbe people of Ghana, and "hiorwe" (literally "sky illness") is characterized by convulsions reminiscent of cerebral malaria and thought to be caused by evil spirits and witchcraft[43]. In Zimbabwe, "nyongo" is a condition associated with mosquito bites which causes fever and headache, a close match with malaria, although some people regard it as a separate disease[41]. Others consider malaria as the result of too much hard work or contact with excessive heat, which can upset an internal hot/cold equilibrium[46], and yet others do not discriminate between malaria and diarrhea[48]. The difficulty in precisely identifying malaria as a separate condition is a hindrance to proper case management where self-treatment is prevalent: if those afflicted do not know what they are ill with, how can they seek proper treatment? Often a trial and error approach is employed, where the diagnosis is changed based on response to self-treatment[43], but the inappropriateness of this strategy is obvious.

The perception of disease etiology may have dramatic effects on treatment outcome. Symptoms of severe malaria, including splenomegaly, anemia and convulsions are widely regarded as the separate disease "ndege-ndege", which is thought to be of spiritual etiology[46]. In these cases treatment is known to be sought at traditional healers, who are believed to be able to deal with the mystical origin of the disease. Sadly it is also believed that injections are lethal to children with ndege-ndege, meaning that many children in this critical state are not brought to formal health care or arrive much too late. The high fatality rate of children with severe malaria in formal healthcare caused by these delays therefore act to enforce the perception of such care as "dangerous"[46][42].

Misconceptions of modern treatment can also be a hindrance in the case of pregnant women, one of the most vulnerable groups. It is widely believed that bitter substances can cause abortion so pregnant women are advised to avoid such substances[46], which includes chloroquine. This is an undesirable effect as antimalarial treatment during pregnancy actually reduces the incidence of miscarriage and improves birthweight[24].

It is clear that there are substantial barriers to achieving targeted and efficient self-treatment, partly in recognition of malaria as a distinct disease and partly in using a correct and full dose of an efficient antimalarial.
7 Evaluation of interventions

Not many studies have demonstrated the effects of microscopy interventions, although one study from Ghana reported an increase in laboratories producing tests of an acceptable quality from 84% to 91% through training interventions[26]. This study was also able to introduce a rudimentary quality control scheme for microscopy, which is encouraging since such schemes are an important tool in proper laboratory management. However this does not address the more important aspect of correct use of laboratory diagnosis.

Also, while it is certainly the case that public health infrastructure in much of SSA is significantly below standard, investments in public health infrastructure are not likely to reach the majority of the population. Areas with high prevalence of self-treatment are often rural communities with little access to health care and low economic elasticity[27][31], and improved diagnostic facilities in clinics which are not accessible to these people are therefore unlikely to improve case management for them.

Available evidence indicates that the existing distribution networks of informal sellers may be effectively targeted in interventions. It has been shown that shopkeepers could be trained through a series of short workshops to give better advice on antimalarial treatment, which raised the purchase of adequate doses of antimalarials from 32% to 83%-90%. Advice on the proper use of drugs based on questions asked by the shopkeeper about the age of the drug user and the symptoms of their illness were given in 94-98% of purchases compared to 2% before the intervention. The actual adherence was slightly lower, with 65%-75% administering the correct dose at home. This should be contrasted with the previous rate of 4%, indicating that the shopkeeper intervention was able to significantly alter not only behaviour of the shopkeepers, who learnt to give proper advice in most cases, but also of care givers who were able to use that advice to dramatically improve drug adherence[49].

Influencing the demand side is thus equally important. As illustrated above there are several local perceptions of the etiology of malaria and these perceptions are likely to influence which treatment is sought. The most urgent requirement is for severe malaria cases to be treated within the public health system within a timeframe that minimizes fatalities. This calls for attitude changes within the population, but results may also be achieved by involving traditional healers. If interventions were directed at educating traditional healers in the same manner as the shopkeepers, they could be trained to recognize severe malaria symptoms and refer such cases to formal care. Whether traditional healers would be willing to compromise their spiritual role in favour of western medicine is an open question, but studies have shown that some healers already refer patients to conventional therapy if their symptoms worsen or the treatment does not seem to be working[44].

Regardless of whether drugs are purchased from informal sellers or health clinics the importance of adherence to a given drug regimen is paramount for the treatment outcome. Numerous studies have shown poor compliance with antimalarial drug courses, much of which is associated with poor knowledge of correct dosage[50]. In Nigeria it was shown that the use of a simple pictorial guideline (fig. 7.1) improved the correct use of chloroquine from
This study relied on solid groundwork identifying the local disease "iba" as malaria, and knowledge of malaria (iba), its symptoms and how cases should be handled was disseminated by "mother trainers", a core group of mothers who were trained by the researchers and acted as teachers to the rest of the mothers in the village.

Apart from community level education on dosage it has been found that packaging of drugs can affect adherence. Many dispensaries supply drugs in a plain envelope or bag with no instructions. Supplying drugs in prepacked age-specific form improved adherence from 61% to 80% in children taking chloroquine tablets, and in a different intervention adding pictorial instructions to packages increased adherence from 37% to 52%, and to 73% if verbal instructions were given as well[50].

Figure 7.1: Pictorial instructions for home treatment of uncomplicated malaria[47]

These results indicate that lack of knowledge and illiteracy are major determinants of adhesion, but also that relatively simple interventions can improve adherence dramatically. Where the costs of these interventions were available from a user perspective, they were either very low (US$0.01 for a pictorial insert) or actually decreased the cost of treatment because fewer tablets were needed[50].

The use of self-treatment can probably ensure treatment within a timely fashion and with proper dosage if relevant interventions are implemented, but this does not change the fact that many non-malarial episodes are still recognized as malaria. If trained professionals are unable to distinguish malaria from alternative diseases based on symptoms alone, those afflicted are unlikely to do any better. The challenge of correctly identifying true malaria cases is more complicated than ensuring drug adherence, because it relies not only on knowledge
but on technical capacity. It has been argued here that the state of microscopes in SSA laboratories is substandard, and a large proportion of the population live too far away to make routine use of the facilities when they are available. This is unlikely to change in the near future, as an upscaling of public health infrastructure towards more numerous and better quality clinics would be a very cost-intensive operation, and the upgrade of roads and public transportation to facilitate access from remote areas is an equally daunting task. However, in the spirit of community training an intervention aiming to educate a small number of village inhabitants in the diagnosis of malaria, pneumonia and other common infections using simple tools such as RDTs and simple clinical algorithms would perhaps allow a greater number of true malaria cases to be identified locally and treated accordingly. Tools for supporting such layman diagnostic practices could integrate local factors such as the local transmission rate, the use of insecticide treated bednets and other simple indicators of the probability of contracting malaria in the setting in question.

8 Discussion and conclusion

It has been argued here that the availability of diagnostic tools to healthcare workers is mostly inadequate, but also that availability does not imply correct use. The effective case management of malaria with the intent of saving expensive antimalarial drugs depends on such correct use, but calls for attitude changes among health care workers. In cases where the irrational prescription of antimalarial drugs are a response to social expectations and the perception that healthcare workers are not doing their job properly if they do not prescribe[44][40], public attitudes also need to be examined and changed.

However, the use of public health facilities and thus access to laboratory diagnosis is unevenly distributed with urban inhabitants enjoying better access than the rural population[51][41]. Since around 50% of the population of SSA live in rural areas[52] and the prevalence of malaria is generally greater here[41], an immediate and far reaching measure to reduce malaria-related morbidity and mortality is to implement interventions in such areas to improve knowledge of self-diagnosis and -treatment.

The national policy of ACT usage in most of SSA[13] is however undermined by self-treatment, as ACTs are usually available primarily via the public sector. Here there is a chance that they may be administered correctly through the use of diagnostic services, but in the informal sector, despite a national policy of ACTs as first line drugs, those treating themselves are likely to continue using outdated antimalarials as reported in Burkina Faso[12]. This is a major obstacle which may not be easily overcome. The light at the end of the tunnel for these people may be the current research in artemisinin production methods, which has recently (June 4th, 2008) announced a new method utilizing genetically modified yeast strains and bioreactors to produce artemisinin at 1/10th the cost. The production is expected to start in 2010 and produce enough artemisinin in 2 years to cover worldwide demand[53], which may make ACTs available through private channels in sufficient amounts.
and at a reasonable cost.

There are many challenges facing the African continent today, and none are likely to be solved in isolation. Malaria is indeed a public health burden, but is also estimated to cause a 1.3% loss of GDP growth[54] and a US$ 12 billion loss in productivity annually for malaria endemic nations[55]. "Poverty leads to ill health, and ill health breeds poverty", in the words of Gro Harlem Brundtland[56], simple words that state the simple reality of malaria and other diseases causing morbidity and mortality and exacerbating poverty. The statement also hints at cross-sectoral issues, in that good health relies on factors such as education, transport infrastructure, access to care and economic capacity to pay for it. The minister of health may press for better clinics or equipment, but he cannot build roads or erect schools. The long term effort to eradicate malaria should thus be seen as part of a broad development issue and not as an isolated measure.
9 Glossary

Anemia Deficiency of red blood cells

Clinical algorithm The process of identifying a series of symptoms and drawing a conclusion of the illness from those symptoms.

Efficacy A measure of how well a drug clears an infection in a clinical setting, in the case of malaria, the ability to clear parasites from the blood.

Endemic disease A disease which is prevalent in a given geographical context.

Etiology The biomedical (or other perceived) cause of a disease, eg. parasite infection.

Parasitemia The presence of parasites in the blood.

Presumptive treatment Treating all cases of febrile illness as though they were malaria.

Recrudescence Reappearance of a treated malaria infection due to survival of parasites in the blood.

Resistance Ability of an organism to survive large amounts of a given drug.

Sensitivity In diagnostics, the percentage of actual cases of an illness identified. High sensitivity corresponds to few false negatives and vice versa.

Splenomegaly Enlargement of the spleen.

Transmission rate The likelihood of becoming infected with malaria within a given context. Commonly measured in % as the proportion of all febrile patients with positive parasitemia.
10 Abbreviations and Acronyms

ACT Artemisinin Combination Treatment
CQ Chloroquine
GFATM Global Fund to fight AIDS, Tuberculosis and Malaria
GDP Gross Domestic Product
GNI Gross National Income
HIV/AIDS Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
RBM Roll Back Malaria
RDT Rapid Diagnostic Test
SP Sulfadoxine-Pyrimethamine
SSA sub-Saharan Africa(n)
UN United Nations
UNDP United Nations Development Programme
UNICEF United Nations Childrens Fund
WHO World Health Organization
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