

**ACCESS TO ANTIMALARIAL MEDICINES**

**IMPROVING THE AFFORDABILITY  
AND FINANCING OF  
ARTEMISININ-BASED  
COMBINATION THERAPIES**



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Malaria Control Department &  
Essential Drugs and Medicines Policy Department

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## 1. INTRODUCTION

Malaria management is in a state of transition. Chloroquine resistance has increased around the world, and this single drug treatment has become useless in most malaria-endemic areas. Resistance to sulfadoxine–pyrimethamine (SP) is also widespread and its use will soon have to be discontinued. Resistance to other antimalarial drugs, such as amodiaquine, varies, but their useful therapeutic life also appears limited. This is unfortunate since these currently used drugs are all off-patent, with low prices close to production costs.

Options for alternative antimalarial drug policies are limited, especially in the regions facing the highest resource constraints, such as Africa, south of the Sahara. In many cases, a lack of resources has forced countries to continue the use of drugs whose effectiveness is known to be limited due to drug resistance. Although the potential value of drug combinations, particularly artemisinin-based combination therapies (ACTs), is widely acknowledged and accepted, high costs are still a major barrier to their effective use. Because of the increasing role as first or second-line treatment of malaria of these drugs, it is important that their use is secured, that they are not misused to the extent of currently available antimalarials, and that the development of resistance is held back as long as possible. (WHO, 2001b).

This paper provides a background for further discussion on affordable and sustainable financing policies for ACTs in the short and medium-term future. It does not prescribe “solutions”, but instead presents a critical overview of the main policy options to improve affordability and financing. It focuses on the current situation and addresses the challenges in improving access to combination therapies in African countries, south of the Sahara, which bear the highest malaria burden and suffer the worst consequences of increasing drug resistance.

There are already standard texts, such as *Managing Drug Supply* (Quick et al, 1997), which describe drug supply systems suitable for developing countries. These texts lay down the principles of good drug management including selection, good procurement practices, efficient distribution, rational use, adequate financing, and functional quality assurance. Unfortunately, few of these texts refer to the particular issues faced by malaria control.

This paper will build on two sets of knowledge and experience — that of WHO/Essential Drug Management in drug financing and affordability, and of Roll Back Malaria in antimalarial drug supply to countries around the world. Consulted documents are listed in the reference section.

Section 2 of this paper discusses current prices of antimalarial drugs, and projections for the future. Section 3 includes information on current antimalarial drug financing mechanisms, and discusses the question “who will pay for ACTs?” Section 4 shows how much consumers already pay for treating malaria, and provides information on the indirect costs of malaria treatment. Section 5 reviews the experiences of other priority health programmes that have worked to improve financial access to drugs. Based on this information, Section 6 discusses options for improving antimalarial drug policies in the worst malaria-endemic countries, particularly those in Africa, south of the Sahara.

An annex giving a price overview of drugs commonly used in malaria control programmes in the regions in the world is included. (Also see <http://rbm.who.int/amdp>).

## 2. CURRENT PRICING OF ANTIMALARIAL DRUGS

Considerable price variations for the most common antimalarial drugs were noted a decade ago in a review of listed sources of pharmaceuticals (Foster, 1991). The clear message was that drug procurement could benefit from careful comparisons of prices from different sources. Today, complete, accurate, and up-to-date price information from international suppliers is readily available from many sources. WHO, for example, publishes a comprehensive list of medicine prices on its website ([www.who.int/medicines/organization/par/ipc/drugpriceinfo.shtml](http://www.who.int/medicines/organization/par/ipc/drugpriceinfo.shtml)). Management Sciences for Health, in collaboration with WHO, issue an annual Drug Price Indicator Guide of essential medicines (MSH 2002, <http://erc.msh.org>), which gives prices and addresses of reputable suppliers who sell at non-profit, world-market wholesale prices. Several of these not-for-profit wholesalers, such as the International Dispensary Association (IDA, [www.ida.nl](http://www.ida.nl)), or UNICEF Supply Division in Copenhagen ([www.supply.unicef.dk](http://www.supply.unicef.dk)), also publish up-to-date price information in catalogues and websites.

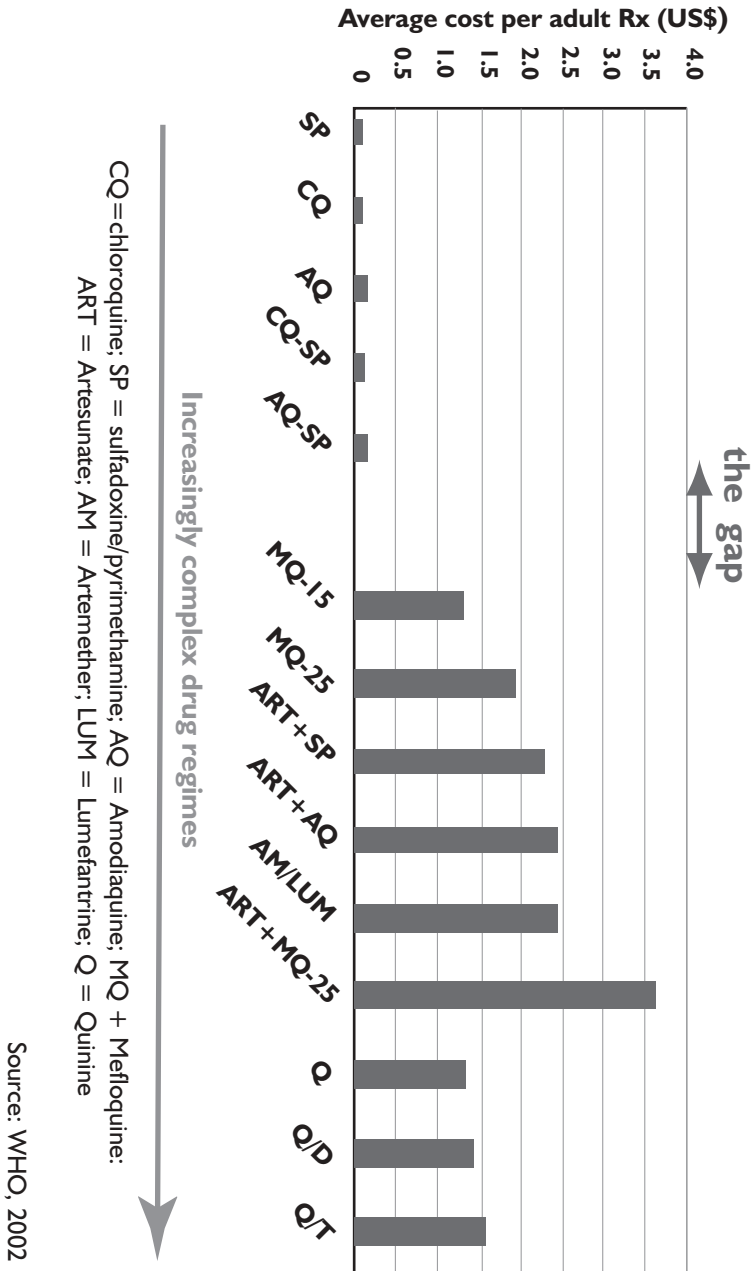
6 The prices of currently used antimalarials have developed according to “free market” mechanisms over the past 10 years, largely because of the availability of comparative information to buyers. Procurement officers can now budget and place orders using this data as stable indicators of likely costs. By introducing large-scale procurement pooling they can further reduce prices.

Unfortunately, the situation is much more complex for the new class of ACTs. With the exception of one co-formulated product (Coartem: artemether–lumefantrine) ACTs are only currently available as blister-packed separate drugs. Secondly, there are only a limited number of suppliers of artemisinin products. Furthermore, the “free market for ACTs is only just beginning to be primed” (Laing & McGoldrick, 2000). This situation may change when demand increases and ACTs become more widely used. Until then, ACTs are likely to have affordability and pricing problems.

The new ACT preparations are currently only available from major suppliers. Annex 1 lists their unit and full-treatment prices, and it is clear that antimalarial treatment costs in the future are going to be much higher than today. Until recently, it cost well below US\$ 1 to treat a case of malaria, but with more complex drug regimes, including ACTs, the cost will rise to several dollars per treatment (see Figure 1).

While reviewing prices, it is important to remember that drug prices to end-consumers can be very different in public and private health sectors. A survey in four East African countries (Myhr, 2000) found that essential drugs are far from equity priced. Myhr concluded that in these countries, pharmaceutical prices were set to “what the market can bear”. Considerable variations were found between generics and their brand-name equivalents, and even between different brands of the same drug. In some cases, retail prices of brand-name drugs were

Figure 1 : Cost of antimalarial options



higher than in European countries. The survey included availability and pricing of Mefloquine tablets, Artemether tablets and Artemether injection. Per-tablet prices of Mefloquine varied from a low of US\$ 0.54 for a generic product in the public sector of Uganda, to US\$ 8.10 for a brand-name product in a private, for-profit pharmacy in the United Republic of Tanzania.

### 3. CURRENT FINANCING MECHANISMS

Public expenditure on malaria prevention and treatment by most African countries, south of the Sahara, is difficult to estimate (Goodman et al, 1999). Governments rarely have specific budget lines for different components of malaria control activities, health facilities do not often separate malaria-related expenditure from other costs, and information from donor-funded projects is mostly buried in unpublished planning and monitoring reports.

It is, however, safe to say that antimalarial treatment costs are a huge burden to both health systems and consumers. One author (Kirigia et al, 1998) estimated that 15% of the annual recurrent costs of inpatient care in a Kenyan district hospital, and 9% in the adjacent sub-district hospital, were due to paediatric malaria admissions. Inpatient treatment costs for severe malaria were US\$ 35 in these hospitals.

As a result of the high malaria incidence in Africa, south of the Sahara, fever is often treated as malaria. Between 20% and 40% of outpatient visits in such countries are for “fever”, while “suspected malaria” among inpatients ranges from between 0.5% to 50% of admissions in different studies (Goodman et al, 1999).

Although accurate figures are hard to obtain, a comparison between Kenya and the United Republic of Tanzania is useful. Kenya spends around US\$ 1 per person per year on malaria control, which represents around 30% of its recurrent health budget. The Ministry of Health meets costs of antimalarial drugs in Kenya with contributions from several donors<sup>1</sup>.

Tanzanian estimates suggest that the country spends US\$ 2.19 per person per year, or 39% of its total health expenditure, on malaria control. One-third of this is spent on drugs. Malaria expenditures are met by households for private sector services (71%), the government (20%) and donors (9%) (Jowett M, personal communication, 2000). Malaria accounts for 30% of the country’s total health burden.

Table 1 compares health, drug consumption and malaria figures for both countries. However it does not include data on the direct and indirect costs of currently “failing” antimalarial drugs, and is therefore not fully indicative of the real difference in health spending on malaria that would be incurred in changing from current first-line antimalarials to ACTs.

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1. Donors include WHO, United Nations Children’s Fund (UNICEF), the UK’s Department for International Development (DFID), World Bank, the Royal Danish Ministry of Foreign Affairs (DANIDA), the US Agency for International Development (USAID), Japan International Cooperation (JICA), the African Development Bank (ADB), the African Medical and Research Foundation (AMREF), US Centers for Disease Control and Prevention (CDC), and Médecins sans frontières (MSF).

**Table 1. Key data on spending for health, drugs and malaria in two selected countries in Sub-Saharan Africa**

	Kenya	Tanzania
Percentage of pharmaceutical spending compared with total health spending, 2000 <sup>a,e</sup>	24%	39%
Private pharmaceutical spending as % total pharmaceutical spending, 2000 <sup>a</sup>	94%	45%
Estimated costs of first and second-line antimalarial drugs <sup>b</sup>	US\$ 850 000	US\$ 572 000 <sup>c</sup>
Estimated cost of inpatient antimalarial drugs <sup>b</sup>	US\$ 500 000	N/A
Estimated cost of SP for intermittent presumptive treatment <sup>b</sup>	US\$ 300 000	N/A
Estimated cost of microscopy requirements <sup>b</sup>	US\$ 350 000	N/A
Estimated cost of ACT (Coartem) treatment based on 10 million cases in each country <sup>d</sup>		US\$ 16 500 000

Source: a. Provisional and unpublished EIP/EDM estimates; b. Malaria Consortium, 2001; c. Goodman et al, 2002; d. assuming that 50% are aged under 5 years, and adult treatment with Coartem costs US\$ 2.40, and paediatric treatment US\$ 0.90<sup>b</sup>; e. Jowett M, personal communication, 2000.

## 4. COST-EFFECTIVENESS IN MALARIA MANAGEMENT

A recent study of the cost-effectiveness of malaria interventions (Goodman et al, 1999; see Figure 2) found that all interventions were attractive options for implementation. Each had a cost per DALY (disability-adjusted life year) averted below US\$ 150, which may be more than some commonly-used health interventions (e.g. measles vaccination, between US\$ 2 and US\$ 17 per DALY averted), but is much lower than, for example, the medical management of hypertension, (more than US\$ 2000). WHO recently redefined the threshold of cost-effectiveness, referring to interventions which have a cost-effectiveness ratio of one to three times per capita income (gross domestic product per capita) as “cost-effective”, and those with a cost-effectiveness ratio less than, or equal to, per capita income as “very cost-effective”.

Interestingly, improving compliance with a first-line antimalarial drug, and improving accessibility of second and third-line drugs were also found to be highly cost-effective, with costs per DALY averted clearly below US\$ 10. Estimates of the cost-effectiveness of ACTs were not included, as little information was available at the time of the review. Goodman strongly recommended further research into the cost-effectiveness of combination therapies.

Results for the cost-effectiveness of malaria interventions were very similar in middle-income countries. The relative cost-effectiveness of interventions remained unchanged, while the actual costs per DALY averted in each case were only slightly higher. For all interventions, the costs per DALY averted ranges were considerably less than US\$ 150 and therefore the current WHO benchmarks for cost-effectiveness.

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## 5. USE, QUALITY AND COSTS OF ANTIMALARIAL DRUGS AT THE CONSUMER LEVEL

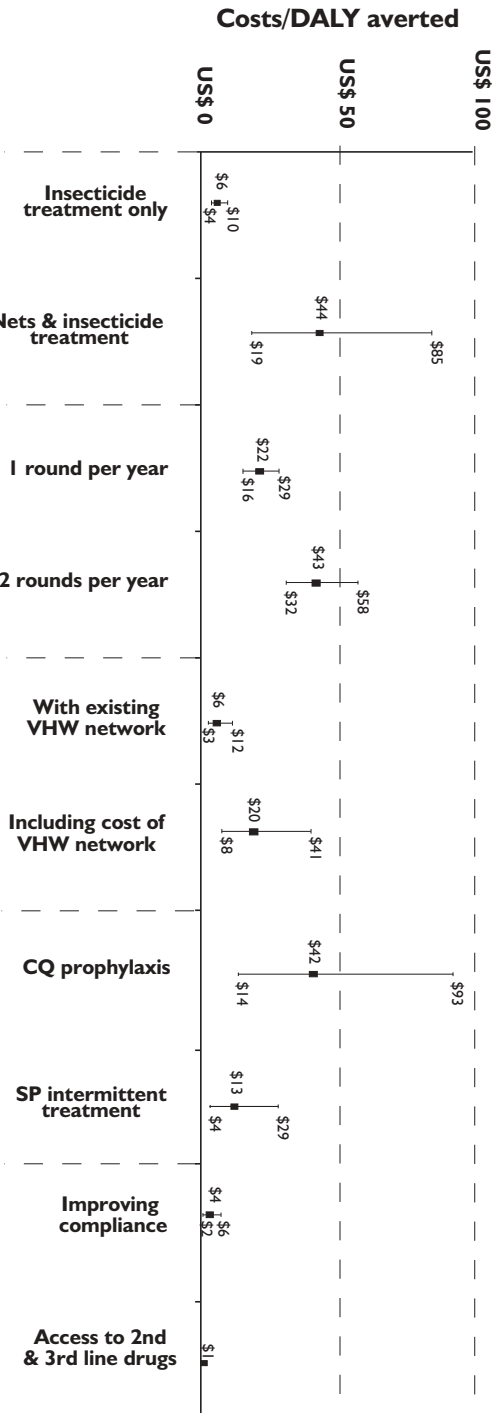
Many malaria cases are treated outside the formal health delivery system in African countries south of the Sahara. Several studies have investigated household management of “fever” in malaria-endemic areas, but at least one (Goodman et al, 1999) cautions against generalizing beyond the original settings of the study. Household expenditure levels are likely to vary from area to area and from season to season with per capita income. Some studies have been conducted in urban areas only; and short survey periods may not have taken seasonal distribution of malaria and cash availability into account. Moreover, definitions of “self-medication” may vary, as well as what are considered “direct” and “indirect” costs associated with malaria.

### 5.1 Household management of malaria

Inability to pay for treatment and a perceived absence of drugs in the formal health delivery system are the main reasons why people do not use public health facilities when they are ill with malaria. A number of studies show that malaria treatment outside the formal health services is a widespread practice throughout Africa, south of the Sahara.

- A review of two urban and eight studies of paediatric cases of malaria in rural areas in African countries found that a median of only 38% of malaria cases were seen in government health centres (Deming et al, 1989).

**Figure 2: Cost-effectiveness of selected malaria interventions in a very low-income country with high transmission: mean and 90% range for the cost per DALY averted (1995 US\$)**



**Notes:**  
*Insecticide-treated nets:* one treatment of deltamethrin a year, no insecticide resistance. *Residual spraying:* lambda-cyhalothrin, Approach 1 to calculate effectiveness, no insecticide resistance. *Chemoprophylaxis for children:* Maloprim, perenatal transmission, no resistance to Maloprim.  
*Antenatal:* Incremental costs, primigravidae only, 50% CQ RII/RIII resistance, 10% SP RII/RIII resistance. *Case management:* gross costs, CQ as first-line drug with 30% clinical failure.

Source: Goodman et al., 1999

- In Togo, 83% of reported fevers were treated at home with an antimalarial drug (Deming et al, 1989).
- In Kenya, 60% of surveyed episodes of febrile illness were treated at home with locally-purchased herbal remedies or medicines, and only 18% went to a health centre or hospital (Ruebush et al, 1995).
- A household survey in Burkina Faso concluded that only 13% of mild episodes and 54% of severe cases of fever were treated by “professional services” (Sauerborn et al, 1991).
- Self-treatment with drugs bought from ordinary shops was commonly reported in a survey in Uganda (Ndyomugenyi et al, 1998).
- A comprehensive, but dated, paper reviewed malaria self-treatment studies in different countries, ranging from a low of 19% in Guinea to a high of 94% in rural Ghana; the average of reviewed studies being about 66% (Brinkmann & Brinkmann, 1991).

## 5.2 Appropriateness of self-medication with antimalarials

Self-administered treatments too often use inappropriate dosages. The findings below warn that self-medication practices have been severely inappropriate with current antimalarials, and are likely to be inappropriate with future antimalarials, unless action is taken now.

- In Togo, 70% of treatments administered at home were found to be of inadequate dosage (Deming et al, 1989).
- A significant proportion (24.6%) of caregivers in a Nigerian study used sub-curative doses of chloroquine to treat children (Ejezie et al, 1990).
- Only 38% of adults in a Zambian study (Makubalo, 1991) knew the correct dosage of malaria treatments for adults, and only 25% for children.
- A survey in Kenya (Kirigia et al, 1998) estimated that only 4% of children given shop-bought chloroquine had received an adequate total dose, while even fewer (2%) received chloroquine over the recommended 3-day period.

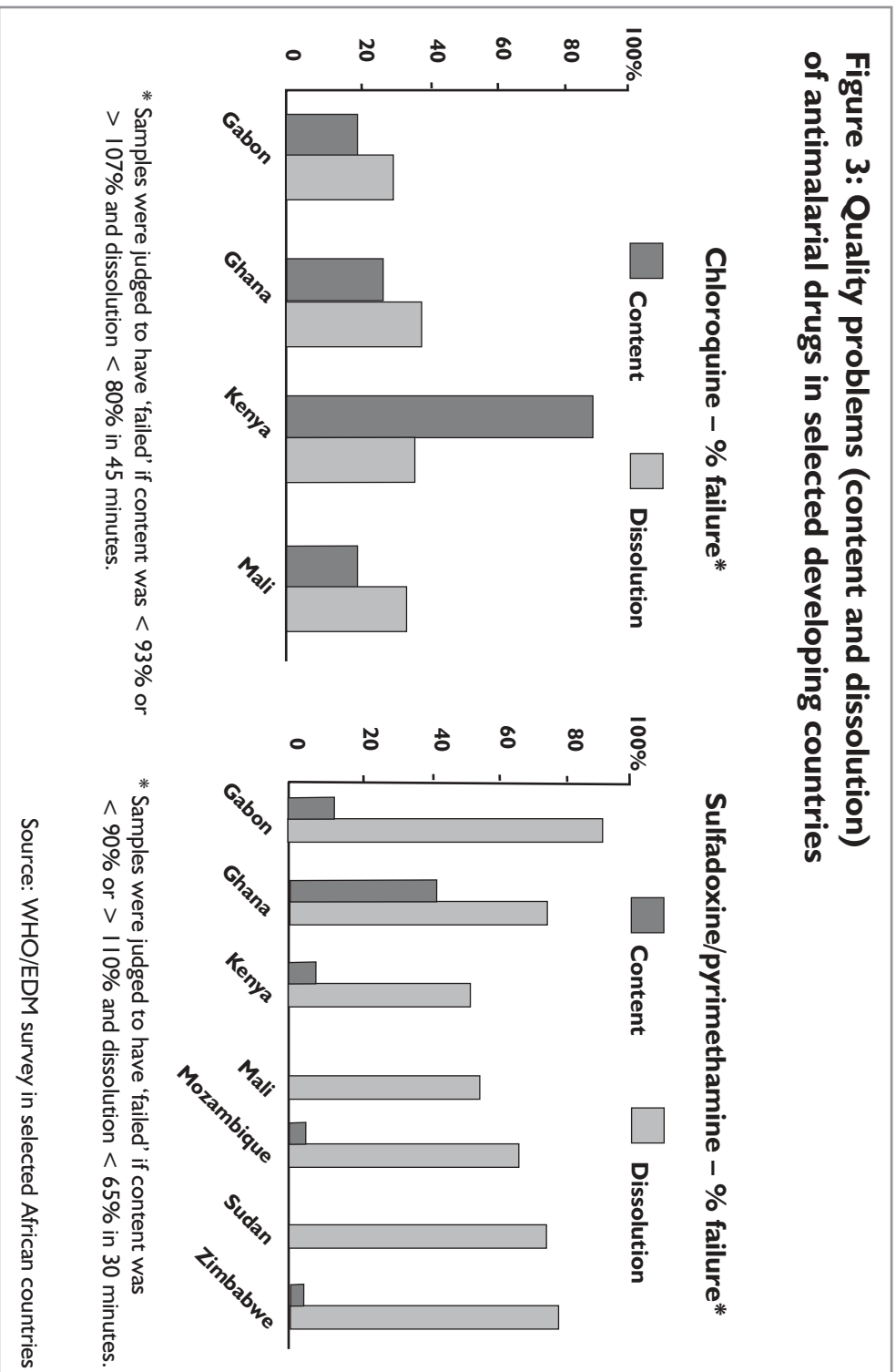
## 5.3 Quality of antimalarial drugs in developing countries

The numbers of substandard and counterfeit antimalarial products circulating in developing countries is an issue of serious concern. Quality of antimalarial drugs differs greatly among countries, both in content and dissolution.

Drug quality is rarely independently verified in most countries and local capacity for drug quality assurance is poorest where the disease burden is highest. Although malaria-endemic countries carry out drug resistance monitoring according to WHO protocols, drug resistance levels are not compared with product quality, which is responsible for treatment failures in the population.

What is sometimes called “resistance” may actually represent drug quality problems (see Figure 3). In addition, substandard and counterfeit pharmaceutical products may also

**Figure 3: Quality problems (content and dissolution) of antimalarial drugs in selected developing countries**



contribute to the emergence of resistance, as their use may result in low bioavailability, which may result in drug under-dosage. This, in turn, may promote the development of resistance.

In an unpublished survey by WHO's Essential Drugs and Medicine department in eight African countries, significant quality problems were detected. The study, which evaluated samples of chloroquine syrup, chloroquine tablets and sulfadoxine–pyrimethamine tablets, found that:

- Active ingredient content failure rates averaged 57%, and ranged from a high of 66%, to a low of 25% for chloroquine syrup;
- Active ingredient content failure for chloroquine tablets was very significant, with highest levels of 66% and lowest 20%; and
- Failure rates for SP tablets were most serious with regard to the dissolution of the pyrimethamine component. Average failure rates were 91.1%, and ranged between 75% to 100%.

It is recommended that action be taken at country level to overcome the problem of substandard and counterfeit drugs. Appropriate measures might include: promoting good procurement practices in the public sector; monitoring and supporting Good Manufacturing Practices (GMP) compliance by manufacturers and suppliers; and supporting the implementation of sound and effective quality control and pharmacovigilance surveillance programmes within Drug Regulatory Authorities to ensure safe use of good quality antimalarial products.

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WHO and other partners have already started a pre-qualification project for artemisinin-based antimalarial products. Dossiers submitted for review are being evaluated for compliance with WHO recommendations and guidelines for assessment of multi-source products (WHO, 1998) as applicable. Manufacturing sites are also being inspected to assess GMP compliance. Products and manufacturing sites that meet these standards will be included in a list of suppliers whose products are considered acceptable in principle for procurement by United Nations agencies. However, if a particular product or supplier is not included in the list it may mean that the supplier of the product had not participated in the process. The list will be reviewed and updated at regular intervals.

#### **5.4 Direct and indirect costs of malaria to households**

Drug costs represent a large, possibly the largest, component of antimalarial treatment. The available evidence shows that household expenditures on malaria-related treatment (fees, drugs, transport and the cost of subsistence) ranged between US\$ 0.39 and US\$ 3.84 per person, equivalent to between US\$ 1.79 and US\$ 25 per household. (Goodman et al, 1999)

- In Malawi it was found that low-income families spent between 28% of household incomes for direct costs of malaria treatment, to only 2% in higher income families. Indirect costs were 3.1% and 2.2% for the same income groups. The financial burden of malaria was much higher in the low-income groups (Ettling et al, 1994).

- In Ghana, the average total treatment cost per malaria episode was US\$ 3.23 for mild cases and US\$ 6.40 for severe cases. The average direct costs and indirect costs (travel and waiting time) amounted to 3.7 days of male output or 4.7 days of female output (Asenso-Okyere & Dzator, 1997).
- In Sri Lanka, average household costs per patient who fully recovered from “malaria” were US\$ 7. Of this, 76% was for indirect costs, with the remaining 24% for cost of medicines and indirect costs. Direct costs were greater for those seeking treatment in the private sector (Attanayake et al, 2000).
- A household survey in Burkina Faso found overall out-of-pocket expenses of US\$ 0.82 for mild episodes of malaria, of which US\$ 0.71 (87%) was for drugs and US\$ 0.11 for travel costs. For severe cases, a total of US\$ 4.21 was spent, of which US\$ 3.49 (83%) was for drug purchases, and US\$ 0.72 for travel. The overall direct cost of malaria was shared unequally between the community (86%) and health system (14%) (Sauerborn et al, 1991).
- A Ghanaian study found that the combined costs of drugs from clinics and drug stores took over 60% of the cost of treatment of fever. As health care facilities generally do not provide all drugs prescribed, a significant amount of the drug cost is incurred at drug stores (Asenso-Okyere & Dzator, 1997).

**Given the findings presented in the preceding paragraphs, it is safe to conclude that:**

- a) Most “malaria” cases are treated at home with home remedies or drugs bought directly from the private sector. It is generally well known that distance to clinics and health centres, frequent stock-outs, and poor services are the main reasons for non-use of public health facilities for antimalarial treatment.
- b) In many countries, it is common practice to treat all cases of “fever” as suspected malaria.
- c) Antimalarial treatment practices are frequently inappropriate and this may have contributed significantly to the current problem of resistance.
- d) There are serious quality problems with antimalarial products circulating in developing countries.
- e) Households incur considerable costs for antimalarial treatment, which may be a major contributor to poverty in some countries. The costs of new ACTs may significantly add to this problem.
- f) Poor and inappropriate use of antimalarial drugs may be continued when the new ACT preparations become generally available, especially since their prices are likely to be high. New and effective approaches will be necessary to promote the appropriate deployment of ACTs.

## 6. EXPERIENCES IN IMPROVING DRUG FINANCING

High costs of new drugs are not unique to antimalarials. Other priority health programmes have been confronted with this problem, and there are important lessons to be learned. The following experiences will be presented below in order to help draw up appropriate strategies for the Roll Back Malaria initiative.

- WHO experiences on options to improve affordability and financing of drugs;
- The specific experience in decreasing the costs of anti-TB drugs in DOTS-Plus programmes;
- The specific experience in pricing antiretroviral drugs: the Accelerated Access Initiative.

### 6.1 General options to improve affordability and financing

Affordable prices and sustainable financing are crucial to ensuring access to medicines in low-income countries. The high prices of the new ACTs give these issues even more importance.

A number of general strategies exist to improve affordability of medicines (WHO 2001a, Grace C, personal communication, 2002). These strategies centre around three distinct issues:

1. How to contain prices, i.e. increase affordability, of MULTI-SOURCE products.
2. How to contain prices, i.e. increase affordability, of SINGLE-SOURCE products.
3. How to develop sustainable drug financing strategies.

Multi-source products are those produced by more than one manufacturer, generally off-patent generic drugs. Single-source products are those for which there is only one manufacturer (i.e. patented products or products that demand such high investments that only one or two manufacturers are willing to make them).

Multi-source products need very different cost-containment strategies to single-source products, and must be considered separately. Strategies for multi-source products (e.g. competitive tendering) are largely ineffective when it comes to single-source products (e.g. patented antiretroviral drugs).

The difference between drug financing strategies and affordability strategies should also be recognized. A country may have obtained affordable drug prices, but if no ministry of finance, donor, or development bank is willing to pay for the drugs, then no matter how affordable they are, it will be the consumer who has to pay out-of-pocket for them. For that reason, countries need to work on designing financing strategies, in addition to improving affordability.

#### Measures to contain prices of multi-source products:

- *Generic policies and generic substitution* aimed at promoting competition.

- *Price information from a variety of sources.*
- *Bulk purchasing, competitive tendering and developing “active purchasing power” and prestige among buyers.* Professional negotiation skills and guaranteed high procurement volumes are of key importance in dealing with suppliers. Combination with differential pricing mechanisms may further reduce prices. Many governments still need to improve their procurement practices and pooling demands appears to have great potential in improving affordability.
- *Price regulation, based on manufacturing or importation costs plus a fixed mark-up for the wholesaler and retailer; control of profit margins; comparison with prices in other countries or other medicines in the same therapeutic category.*

**Measures to contain prices of single-source products:**

- *Differential pricing for low-income countries, defined as pricing based on ability to pay.* Producers may demand market segmentation as a crucial pre-condition to engage in voluntary differential pricing. A main concern for companies is unauthorized re-export of low-cost drugs from low-income countries to high-income countries.
- *Bulk purchasing (as above), can also achieve reductions in the price of single-source drugs where larger volumes and longer horizons may be guaranteed.*
- *Voluntary, bilateral price agreements between producers and buyers.* There are numerous concerns with these agreements, including lack of transparency, an anti-competitive tendency (raising barriers to entry for generic firms), and high transaction costs relative to benefits gained. The impact of voluntary agreements on access has been limited to date.
- *Voluntary licences for manufacturing specific drugs.* Firms may voluntarily license patents to companies other than their affiliates. So far there is only one example of a voluntary licence for differential pricing purposes: GlaxoSmithKline’s licence of three antiretrovirals to a South African firm.
- *Compulsory licences for manufacturing specific drugs.* Compulsory licensing has proved an effective bargaining counter for developing countries in negotiating reduced prices with patent holders. The Doha Declaration allows the least developed countries to delay implementation of patent protection on pharmaceuticals until 2016, but as most developing countries already observe patents, this extension has little meaning to poor countries.
- *Patent waivers.* This mechanism has been proposed to limit patent holders’ right to sue for patent infringement in the least developed countries for manufacturing drugs for defined “global” diseases. With the exception of Coartem, artemisinin compounds are not patented, and the patent waiver mechanism is not likely to help much in reducing prices of ACTs.
- Price controls may be effective in reducing prices, but they may also result in products being withdrawn from the market, thereby reducing broader access. The impact of price controls on research and development could be negative for specific product lines.

While it is important to secure the best possible price for essential medicines, price should not be the only basis for recommending or not recommending a particular medicine. Prices can, and do, change. A medicine's price needs to be considered alongside its effect on health outcomes, and it must be compared with the closest available alternatives. In this way the decision-making focus is on value for money rather than the price of any one medicine.

#### Measures to develop sustainable drug financing strategies

Drug prices determine their affordability to governments and consumers, but finance availability determines whether they can be bought at all. Financing must be sustainable and a number of key principles have been identified to help develop sustainable financing policies (WHO 2001a):

- *Optimizing use of government funds* in providing health care and drugs. Government subsidies are frequently “captured” for urban areas and for more affluent populations. Public spending is one of the biggest potential single sources for health funding, and making the best use of public funds is important in developing a financing strategy.
- *Measures to improve efficiency and reduce waste.* Efficiency improvements are a prerequisite when expensive medicines, such as ACTs, are going to be introduced. The principles of improving drug management practices are well explained elsewhere (Quick et al, 1997).
- *Insurances (or “pre-payment” schemes)* are designed to protect populations from the catastrophic financial consequences of health problems, including any necessary drugs. Such schemes include social security, compulsory social health insurance, private health insurance and employer insurances, managed care (linking health care providers to insurers), and small-scale community health insurances. Special arrangements for rural and low-income populations may be included. Insurance systems must be built on the principle of the sick being subsidized by the healthy and the well-off subsidizing the poor (implying that all groups have to be included). However, the availability of insurance schemes in most malaria-endemic countries of Africa, south of the Sahara, is limited and they may not provide a significant mechanism for financing ACTs in the short- and medium term.
- *Cost-sharing mechanisms* may have a place in increasing services financing, but only if equity principles are respected and care is taken that unaffordable costs do not prevent the poor from using the services. Revolving drug funds and community drug schemes operate in scores of developing countries, but only those with strong exemption and other protection mechanisms, good management, community supervision, and phased implementation have continued to operate and maintain their volume of use. Expectations that the costs of ACTs can be largely met by user fees are unrealistic (Creese & Kutzin, 1995) and in any case the adoption of user-fees and cost-recovery mechanisms is uneven. Paradoxically, such schemes are mostly applied in African countries, south of the Sahara, where the burdens of malaria and poverty are highest. Most malaria-endemic countries outside that area provide free treatment for malaria through their public health services (See Table 2).

**Table 2. Public sector financing strategies of antimalarial drugs in selected developing countries**

	<b>Free treatment available</b>	<b>Cost recovery/cost sharing</b>
<b>Sub-Saharan Africa</b>	Botswana, Djibouti, Namibia, South Africa, Swaziland	Angola, Benin, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Democratic Republic of Congo, Côte d'Ivoire, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Guinea, Guinea-Bissau, Kenya, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Somalia, Sudan, United Republic of Tanzania, Togo, Uganda, Zambia, Zimbabwe
<b>Non sub-Saharan Africa</b>	Afghanistan, Algeria, Argentina, Armenia, Azerbaijan, Bangladesh, Belize, Bhutan, Brazil, Cambodia, China, Colombia, Costa Rica, Dominican Republic, East Timor, Ecuador, Egypt, El Salvador, Georgia, French Guiana, Guatemala, Guyana, Honduras, India, Indonesia, Islamic Republic of Iran, Iraq, Democratic People's Republic of Korea, Korea, Kyrgyzstan, Malaysia, Mexico, Mauritius, Morocco, Myanmar, Namibia, Nepal, Oman, Pakistan, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Saudi Arabia, Solomon Islands, Sri Lanka, Suriname, Syria, Tajikistan, Thailand, Turkey, Turkmenistan, United Arab Emirates, Vanuatu, Venezuela, Viet Nam, Yemen	Haiti, Lao People's Democratic Republic, Nicaragua

- *External financing (e.g. donor grants or developmental loans).* External funds are often seen as a viable way of financing health-related expenditure in developing countries. Whether this assumption is justified or not is outside the scope of this paper. However, recipient countries are increasingly demanding determination over the allocation of development assistance, a desire that is recognized and granted by donors. Donors are moving away from providing earmarked funding and are less willing to pay for consumable items, such as antimalarial drugs.

This trend will affect more traditional ideas about raising money “for” malaria. Sustainable financing will require multiple approaches, and the recognition that antimalarials (like anti-TB drugs) cannot be allowed to be marginalized in financing programmes.

## 6.2 Decreasing the costs of second-line anti-TB drugs in DOTS-Plus programmes

The affordability, availability and quality of second-line anti-TB medications have been key factors in the success of DOTS-Plus programmes around the world. To draw up a rational procurement strategy for these drugs, WHO established a Working Group (Gupta et al, 2001; WHO 2000b). The group recommended consolidating the buying side of the market and promoting access to drugs at negotiated preferential prices to projects with adequate technical capacity.

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This pooling approach, combined with professional negotiation skills, resulted in major cost reductions that were sustainable in the long-term. A stepped process was used:<sup>1</sup>

- 1) Using quality-assurance criteria, a comprehensive list of manufacturers was prepared for three categories of drugs, i.e. drugs for which the manufacturer has a monopoly status as patent-holder; drugs where the manufacturer has a monopoly status without a patent; and those in which multiple manufacturers are involved. Negotiation strategies were determined according to the market status of each drug.
- 2) Médecins Sans Frontières was selected as the single negotiator for all parties, and to supply technical support and advance capital.
- 3) Two markets were discussed with the industry. One constituted countries and organizations that had made firm financial and programmatic commitments to establishing pilot projects; the second, based on the estimated number of new multi-drug resistant TB cases globally, included countries assessed on the basis of their need for anti-TB drugs and their intention to join DOTS-Plus. Estimates were made for the consumption of drugs in these markets.
- 4) The needs in the first market were procured through a strategy of direct negotiation, based on quality and price criteria. For the second market, a “tiered-tender” approach

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1. Detailed methodology available at [www.sciencemag.org/cgi/content/full/1061861/DC1](http://www.sciencemag.org/cgi/content/full/1061861/DC1)

was developed, giving a large percentage of the order to the quality-assured company with the lowest-priced drug and a proportional percentage to one or a few of the remaining quality-assured manufacturers.

- 5) The advantages to suppliers were highlighted, including the pooled-procurement and the single-client process for global demand; participation in a high-profile partnership; and the assurance that the usefulness of a drug would not be lost by creating more resistance.
- 6) Access to the preferentially-priced drugs is only given to projects that commit to the recommendations for establishing DOTS-Plus pilot projects. Clearance is given by a multi-institutional body known as the Green Light Committee, consisting of major donors and collaborating agencies.

The strategy dramatically increased supply and decreased the cost of quality-assured second-line anti-TB drugs. It was estimated that countries would save over 90% of their expenditure on second-line anti-TB drugs, if current trends continued. Countries with an established TB control programme and with budgets that include the purchase of second-line drugs could save more than 50% of their overall budget for TB control.

### **6.3 Decreasing the costs of antiretroviral drugs: the Accelerated Access Initiative**

In 2000, five United Nations organizations entered into partnership with five international pharmaceutical companies to improve affordability of HIV medicines and increase access to HIV/AIDS care and treatment in developing countries. The initiative was called the Accelerating Access Initiative (AAI)<sup>1</sup>.

Although 80 countries initially expressed interest in AAI, only 19 finally negotiated new agreements for the supply of ARV drugs with the pharmaceutical companies<sup>2</sup>. Each of these countries was required to create two new entities:

- A national HIV/AIDS drugs advisory board, under the minister of health, composed of representatives of the local medical, public health and HIV/AIDS communities;
- A not-for-profit company to act both as a clearing-house for placing orders for drugs, as well as the channel for subsidies from the companies. This company was funded by AAI's participating pharmaceutical companies.

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1. AAI's founding members were the United Nations Population Fund (UNFPA), UNICEF, WHO, World Bank, and UNAIDS Secretariat; Boehringer Ingelheim; Bristol-Myers Squibb; GlaxoSmithKline; Merck & Co; and Hoffmann-La Roche — later joined by Abbott.

2. Barbados, Benin, Burkina Faso, Burundi, Cameroon, Chile, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, Honduras, Jamaica, Mali, Morocco, Romania, Rwanda, Senegal, Trinidad and Tobago, Uganda, and Ukraine.

By the end of 2001, the costs of ARV drugs offered by AAI's pharmaceutical partners had decreased significantly, in some cases to 10–20% of their price in industrialized countries. Price developments of ARVs in Uganda are presented in Figure 4 (from WHO & UNAIDS, 2002).

It should be noted that the number of patients enrolled in the AAI scheme has gradually increased in recent years, but only after prices fell dramatically. Figure 4 also shows the number of patients enrolled in treatment schemes in Uganda (Ochola D, personal communication, 2002).

AAI claimed that the dramatic price decreases were a direct consequence of its activities, but as explained below, concurrent developments in the global and national access arena contributed significantly. Factors that concurrently led to the fall in the price of ARVs at both the international and national level include (Ochola, 2002):

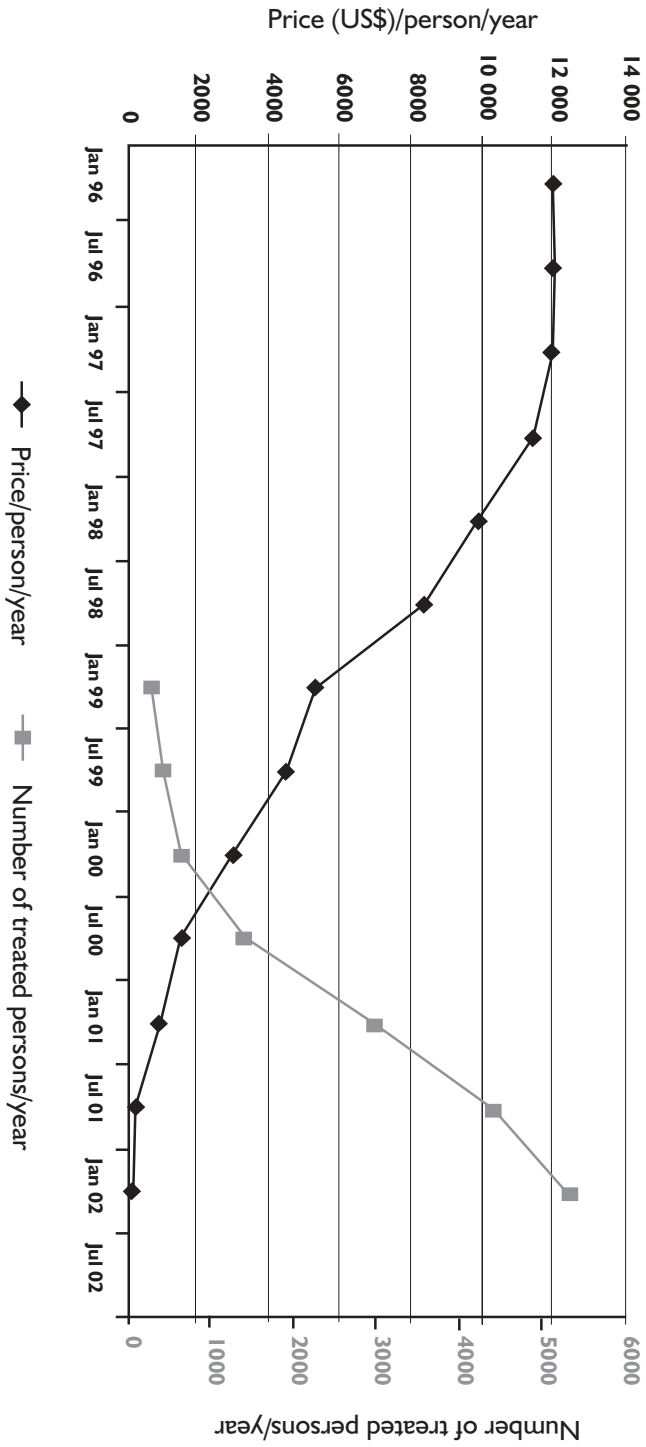
- International outcry/appeal by governments, especially from developing countries.
- Pressure on research-based pharmaceutical industries from activist groups.
- Competition among pharmaceutical industries.
- Increased demand for ARVs as news of their effectiveness spread.
- Generic competition.
- Combination formulation of drugs.
- Increasing variety of ARVs.
- Less complicated drug regimens.
- Increased outlets for ARVs.
- Reduction in laboratory monitoring costs.

Factors that influenced national ARV prices in Uganda included:

- New combination drug products that became available on the market, forcing prices of single drugs to drop.
- Price reductions that were negotiated with multinational pharmaceutical manufacturers.
- Increasing pressure from governments, people living with HIV/AIDS and other activists.
- Changes in the Uganda shilling exchange rates against major currencies, leading to fluctuations in costs of treatment to the patient.

The Uganda report concluded that, at the individual level, price decreases might have had dramatic short-term or long-term effects on affordability and, therefore, sustainability of therapy. However, despite these decreases, prices in Uganda are still far above what most people living with HIV/AIDS can afford.

**Figure 4: Price reductions of a first-line ARV regimen and cumulative enrolment of patients in the Drug Access scheme in Uganda (on generics or branded ARV treatment)**



Source: Modified from WHO & UNAIDS 2002 and Ochola D, personal communication, 2002

## 7. DISCUSSION AND CONCLUSIONS

Drug treatment is vital to any strategy to roll back malaria. Protection and prevention are important, but the morbidity and mortality of malaria in Africa cannot be significantly reduced without effective curative measures.

To date, antimalarial drugs have been cheap, and very affordable to low-income populations. While stock-outs in public health facilities are unfortunate, they are often accepted because cheap antimalarials are readily available in the private sector – even though their quality is often substandard and their use likely to induce resistance. New, effective drugs now exist, but they are expensive and governments are unlikely to be able to finance adequate supplies for their health delivery systems. Private sector prices will be out of the reach of low-income populations.

Increasing rates of resistance mean that continuing efforts to control malaria with the low-cost drugs currently available is no longer an option. ACTs will have to be made widely available in both public and private sectors in malaria-endemic regions of the world. To do this, affordability and financing issues will have to be appropriately addressed.

Improving affordability raises some important questions including which ACTs should be recommended. Costs and drug use practices must be considered as well as the pharmacotherapeutic viewpoint. Then there is the question of improving affordability and increasing available financing for ACTs in developing countries.

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The questions can only be answered by an integrated and collaborative approach, involving ministries of health, NGOs, donors, international agencies and consumers.

### 7.1 Drug use practices and behaviours in malaria management

Current behaviour patterns in the use of antimalarials by consumers and caregivers must be taken into account when considering treatment policies. The affordability and financing of drugs is also directly related to the ways in which drugs are used and should be an integral part of any discussions on selecting treatments. Unaffordable antimalarials may result in poor treatment practices, which contribute to the development of resistance and shorten the useful treatment life of the drug(s).

A major finding of this survey has been that only a limited amount of data is available on the various factors that influence the use of antimalarials. There are large gaps in our knowledge and this document can only “scratch the surface” of the problem. Much more research, involving the global research community, is needed.

### 7.2 Selecting the most appropriate ACTs

Three available ACT combinations have been evaluated for safety and efficacy and are recommended for deployment (WHO 2001c):

- artemether–lumefantrine (Coartem)
- artesunate (3 days) plus amodiaquine
- artesunate (3 days) plus SP in areas where SP efficacy remains high.

Selecting the most appropriate ACT involves technical discussion, but also raises financing and affordability questions. WHO has reached an agreement with Novartis for differential pricing of Coartem (artemether–lumefantrine) for use by public sectors in malaria-endemic countries. The cost of Coartem to developing countries is US\$ 2.40 per adult treatment. This is much lower than in industrialized countries (US\$ 40), but still high for low-income countries, especially when the scale on which the drug needs to be deployed is considered.

Prices of other ACTs may decrease in the next few years, as demand, production and competition increases. MSF (Kindermans et al, 2002) investigated prices from artesunate manufacturers in various countries, and found that they ranged from US\$ 0.63 to US\$ 1.50 for the 600 mg artesunate dose. The cost of the artesunate plus amodiaquine combination was estimated at around US\$ 1.30 per adult treatment today, but was expected to fall to just US\$ 0.60 by 2004.

A study conducted in Burundi, Kenya, Rwanda, the United Republic of Tanzania, and Uganda provides an example of the considerable financial implications of antimalarial drug selection (Kindermans et al, 2002). Costs involved in switching drug choices to artesunate plus amodiaquine-based combination protocols were estimated in these countries. Based on current drug prices, it was calculated that the supplementary cost of implementing the artesunate plus amodiaquine combination (rather than the intermediate solution of amodiaquine plus SP) would be US\$ 1.05 per adult treatment. As prices of the amodiaquine plus artesunate combination are expected to fall, the incremental costs per treatment are expected to decrease to US\$ 0.35 by 2004.

With an estimated 1.2 million cases of malaria per year, the additional cost for Rwanda would therefore be US\$ 945 000 per year, while in the United Republic of Tanzania, with an estimated 8.6 million cases per year, the additional annual cost would be US\$ 6.4 million. The total number of annual malaria cases in the five countries was estimated at 25.3 million and the combined additional cost of deploying the amodiaquine plus artesunate combination in these five countries would be US\$ 19.1 million per year at 2003 prices.

This figure would go down by two-thirds if prices fall as expected over the next few years. Changing to Coartem, priced at US\$ 2.40 per adult dose, would result in a supplementary cost of US\$ 39.2 million for the five countries combined. Coartem is patented until 2010 and prices may not fall as quickly as for other ACT options.

However, the real costs of the continued use of failing antimalarial drugs, including management of treatment failures, management of severe malaria, and transmission control expenses, are not included in these figures, nor is the inestimable cost of poverty and human suffering caused by malaria-related deaths and disability.

### 7.3 Making ACTs more affordable

No single strategy is likely to solve the problem of ACT availability. A pluralistic approach using several strategies to serve different needs and different groups is likely to achieve the best results. Options need to be evaluated and a careful mix of strategies selected.

When health systems are not able to provide ACTs at little or no cost, consumers may have to purchase them in the private sector. Private sector marketing of ACTs may result in unaffordable prices, which may result in use of suboptimal doses, ineffective treatments, partial sales of course-of-treatment packages, poor patient information, increased chances of developing resistance, and perhaps ultimately to increased malaria deaths. The public sector will, therefore, have to take the lead in ensuring access to ACTs. It may also be necessary to regulate the private sector to make ACTs more available and affordable to populations.

### 7.4 Securing sustainable financing for ACTs

Although Ministries of Health rarely make clear how antimalarial drugs are being financed (Goodman et al, 1999) optimizing government subsidies and avoiding the major part of them going to urban centres and better-off populations is a first strategy for ensuring equal access to antimalarial drugs, including ACTs. However, government subsidies are still unlikely to be sufficient for effective malaria control, and donor consortia will be needed to help finance antimalarial drug supplies. New ways of working together will be required. In Kenya for example, a large number of donors fund a great variety of programme activities with limited coordination (Malaria Consortium, 2001) but this traditional “patchwork” funding for malaria control will have to be replaced with more effective cooperation.

Integrated drug financing programmes will have to be designed; collaborations set up between ministries of health, NGOs, and donors; and joint financing mechanisms will have to be designed so that volume purchases can be made and markets forced to provide favourable prices.

One option may be to set up a malaria drug facility, possibly integrated with existing mechanisms such as the Global Drug Facility. This would allow global projections of malaria drug needs to be based on the requirements of endemic countries; drug manufacturers to be pre-qualified to assure manufacturing and production quality; and pharmaceutical prices negotiated with suppliers on the basis of pooled market demands. An integrated and collaborative approach by all stakeholders and the availability of an effective operational budget would be key in setting up such a malaria drug facility.

### 7.5 The need for an integrated and collaborative approach

Reducing the global burden of malaria disease and death, which is most suffered in African countries, south of the Sahara requires a major and concerted effort. A significant component of that effort must be to make effective antimalarial drugs accessible to people

at risk. This is an uphill task since many of the conventional, affordable drugs are no longer effective. The new recommended ACTs are only just beginning to be used in countries, particularly in Africa, and their availability is limited, and costs high.

To make these drugs generally available will require a committed market, plans to scale up the availability and growth of the natural source plant, as well as production of the artemisinin derivatives. In the longer-term, it will require the chemical synthesis of artemisinin analogues. Currently, one of the most limiting factors in achieving these is inadequate financial investment. It is clear that in the short and medium-term at least, considerable donor investments, in the range of billions of US dollars will be required (Sachs, 2002) to ensure that effective quality antimalarial treatments are available where they are most needed.

International and partner cooperation is needed to prime a dormant market and increase the availability of ACTs. Collaboration is required to estimate market size, and pooled procurement mechanisms must be entered into to lower prices. Increased financial support for improving access to antimalarial treatment must be a part of a comprehensive strategy that addresses all of the health systems issues identified in this paper, ranging from national regulatory systems and health financing to education of mothers to improve their adherence to treatment schedules.

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**Annex: Prices of antimalarial drugs from various sources**

Drug	Dosage form (unit)	MSH/WHO <sup>1</sup> 2001	WHO/HQ median <sup>2</sup>	Price/unit (US\$)						
				WHO/AFRO <sup>3</sup>	UNICEF	IDA <sup>4</sup>	Minimum (of all sources, 2001 or later)	Median (of all sources 2001 or later)		
Armodiaquine	150-200 mg (tab)	0.0168	0.0166	0.0152	–	–	0.0152	0.0166		
Artesunate	50 mg, tab	–	0.168	–	–	0.3742	0.168	0.2711		
Artesunate	200 mg, tab	–	0.63	–	–	–	0.63	0.63		
Artemether	80 mg/ml, inj 1 ml	–	0.95	–	–	0.954	0.95	0.952		
Chloroquine phosphate <sup>5</sup>	10 mg/ml, pow for syr, ml	0.0062	–	–	–	0.0019	0.0019	0.0041		
Chloroquine phosphate	10 mg/ml, syr, ml	–	0.0078	0.004	0.004	0.0047	0.004	0.0044		
Chloroquine phosphate	150 mg, tab	0.0098	0.0048	0.0124	0.005	0.0059	0.48	0.0059		
Mefloquine <sup>6</sup>	250 mg, tab	1.5738	0.3071	1.1029	0.3902	0.4	0.3071	0.4		
Quinine dihydrochloride	250-300 mg/ml, inj 2 ml	0.142	0.1182	0.1914	0.107	0.149	0.107	0.142		
Quinine sulphate	300 mg, tab	0.055	0.0229	0.0406	0.0256	0.0305	0.0229	0.0305		
Sulfadoxine/Pyrimethamine	500+25 mg, tab	0.0603	0.0182	0.017	0.0176	0.0215	0.017	0.0182		

Artemether-Lumefantrine (Coartem®) For developing countries only. To be ordered from WHO (see <http://mosquito.who.int/docs>).

1. Management Sciences for Health, WHO. International Drug Price Indicator Guide 2001. Median values of the listed prices are presented.

2. World Health Organization Geneva. Median of drug prices offered by various suppliers 2002.

3. World Health Organization, AFRO 2000.

4. IDA Amsterdam, Netherlands. Prices quoted in Euro (assumed exchange rate: Euro 1 = US\$ 1).

5. The quinine total treatment is less easy to calculate, as patients are mostly moved to oral treatment as soon as possible.

6. Not recommended anymore for Africa (by WHO).

For your notes

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