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Rolling Back Malaria

*M*alaria and underdevelopment are closely intertwined. Over 40% of the world's population live where there is a risk of malaria. The disease causes widespread premature death and suffering, imposes financial hardship on poor households, and holds back economic growth and improvements in living standards. It is time for a major attack on malaria. Roll Back Malaria is a new, health sector-wide partnership to combat the disease at global, regional, country and local levels. Its strategy is outlined at the end of this chapter.

The Challenge of Malaria

Malaria flourishes in situations of social and environmental crisis, weak health systems and disadvantaged communities. Its ability to develop resistance makes malaria a formidable adversary. Effective interventions are available but they are not reaching the people with the greatest burden of malaria because the capacity for malaria control is inadequate in endemic countries, where health systems are often weak. Better use must be made of current knowledge, new products and state-of-the-art technologies to overcome the barrier to human progress which malaria poses.

The health burden

Almost 300 million clinical cases of malaria occur worldwide each year and over one million people die (see Annex Table 8). Almost 90% of these deaths occur in sub-Saharan Africa, where young children are the most affected. Malaria is directly responsible for one in five childhood deaths in Africa and indirectly contributes to illness and deaths from respiratory infections, diarrhoeal disease and malnutrition. Though malaria is still a big problem, huge progress has been made since the beginning of the century; its recent resurgence in Africa contrasts dramatically with the global decline in mortality since 1900 (see Box 4.1).

The rapid spread of resistance to antimalarial drugs presents a potentially devastating threat to effective treatment. Safe, effective and affordable options are quickly running out, and the discovery of new antimalarials is not keeping pace. For decades chloroquine was the main drug used, but increasing resistance forced its replacement in parts of Asia and South America during the 1980s, and in the 1990s African countries are starting to follow suit.

If malaria is diagnosed and treated promptly the infection may quickly subside, but without effective treatment, severe complications – such as cerebral malaria, severe anaemia or multiple organ failure – can rapidly develop, leading to case fatality rates of 10–30%. The progression from mild symptoms to death can be rapid. Mortality is not the only problem. With hundreds of infective bites per person/year leading to frequent illness, morbidity is high. Serious long-term neurological disabilities are experienced in 10% of children hospitalized in Kenya with severe malaria. Less obvious disabilities, including impairment of cognitive development, are probably even more common.

The scale of the problem in many countries appears to be increasing. Furthermore, the number of malaria epidemics is growing both because of climatic and environmental

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Box 4.1 Malaria-related mortality in the 20th century

During the first half of the 20th century the world sustained around 2 million deaths from malaria each year, most in the Asian and the Pacific tropics, and somewhat fewer in Africa. Following the end of the Second World War, national malaria control campaigns were initiated or intensified in the most affected countries, from the Middle East, through the Indian subcontinent and South-East Asia to the islands of the Western Pacific, including those of Indonesia and the Philippines. Using DDT spraying of homes (a method intended to attack the mosquito vectors of malaria where they contact the human host), spectacular reductions in malaria incidence and malaria-related mortality were achieved, especially in India and Ceylon (now Sri Lanka). The zenith of success was reached by the mid-1960s. In subsequent decades, however, the economic and political costs of sustaining the intensive efforts involved in the initial campaigns, combined with emerging resistance of the parasites and their vectors to the chemicals used to attack them, led to the resurgence of malaria transmission throughout southern Asia and the Western Pacific. Most damaging has been the emergence of multi-drug and chloroquine resistant *Plasmodium falciparum*, which, starting in the mid-1960s, has spread outwards from a focus in South-East Asia. Notwithstanding these serious setbacks, a return to the previously high malaria-related mortality rates within this vast sec-

tion of the human population has never been remotely approached. The sustained reduction of malaria-related mortality in a region from the Mediterranean to the Western Pacific in the second half of the 20th century has been an outstanding, if precarious, success in the improvement of human health.

In China, the emergence of a strong national government shortly after the end of the Second World War, and the absence of warfare itself, must have contributed to significant reductions of the malaria burden in the decades that followed. However, political turmoil within China at first prevented major advances. Then in the mid-1970s, a determined anti-malaria campaign was initiated which integrated vector control with rigorous malaria case detection and treatment. Malaria-related deaths in China are now about one

hundred per year compared with the hundreds of thousands per year through the early decades of the century. An important outcome of the Chinese anti-malaria campaign has been the development of the artemisinin derivatives of quinhaosu, a traditional Chinese herbal medicine, to combat chloroquine-resistant *P. falciparum*. In Asia and particularly in Viet Nam in the early 1990s, the use of artemisinin derivatives has dramatically reversed the general rise in malaria mortality rates in the region.

By contrast relatively little effort has been put into trying to control the malaria situation in sub-Saharan Africa. The reasons are several. In the early part of the century, African malaria was a minor part of the global problem. This was because adults in African populations were apparently unaffected, malaria-related morbidity and

mortality being limited to young children – the effect of intense infection rates leading to death or full protective immunity by mid-childhood. At a practical level, however, the intensity of malaria transmission in sub-Saharan Africa, through hugely efficient mosquito vectors, and the poverty and size of the countries facing the problem, meant that large reductions in malaria-related mortality were thought unattainable by means largely based on vector control, which were being used successfully elsewhere.

Nevertheless, malaria-related deaths in Africa, which can never have been fewer than hundreds of thousands per year, did show evidence of per capita decline from the 1950s to the early 1980s. This can probably be attributed to slowly improving living conditions and access to cheap and effective chloroquine. However, the slow downward trend in malaria-related mortality in Africa seems to have undergone a reversal, starting from the late 1980s. In relation to total population, the numbers of childhood deaths from malaria in Africa may, at the very end of the 20th century, be substantially higher than they were 10 years previously. The factor most likely to underlie such an increase in malaria-related mortality rates is the spread of chloroquine-resistant *P. falciparum* across Africa.

Malaria mortality annual rates since 1900

Contributed by Richard Carter, University of Edinburgh, Scotland.
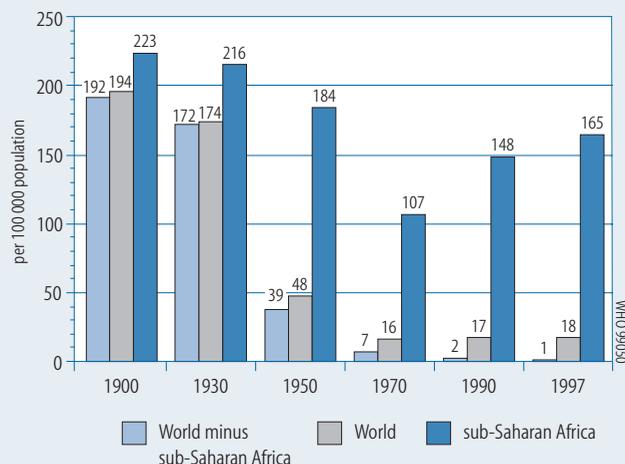
changes, and as a result of human migration, often caused by military conflicts and civil unrest.

THE ECONOMIC BURDEN

Malaria-endemic countries are some of the world's most impoverished. Malaria causes nearly 250 times more deaths in the world's poorest countries than in the richest. The economic burden of malaria to households can be extremely high. Even in the poor countries of sub-Saharan Africa, households have been found to spend between $2 and $25 on malaria treatment, and between $0.20 and $15 on prevention each month *(1)*. Treatment costs of malaria for small farmers have been estimated to be as high as 5% of total household expenditure in Kenya and 13% in Nigeria. Many are simply too poor to be able to pay for adequate protection.
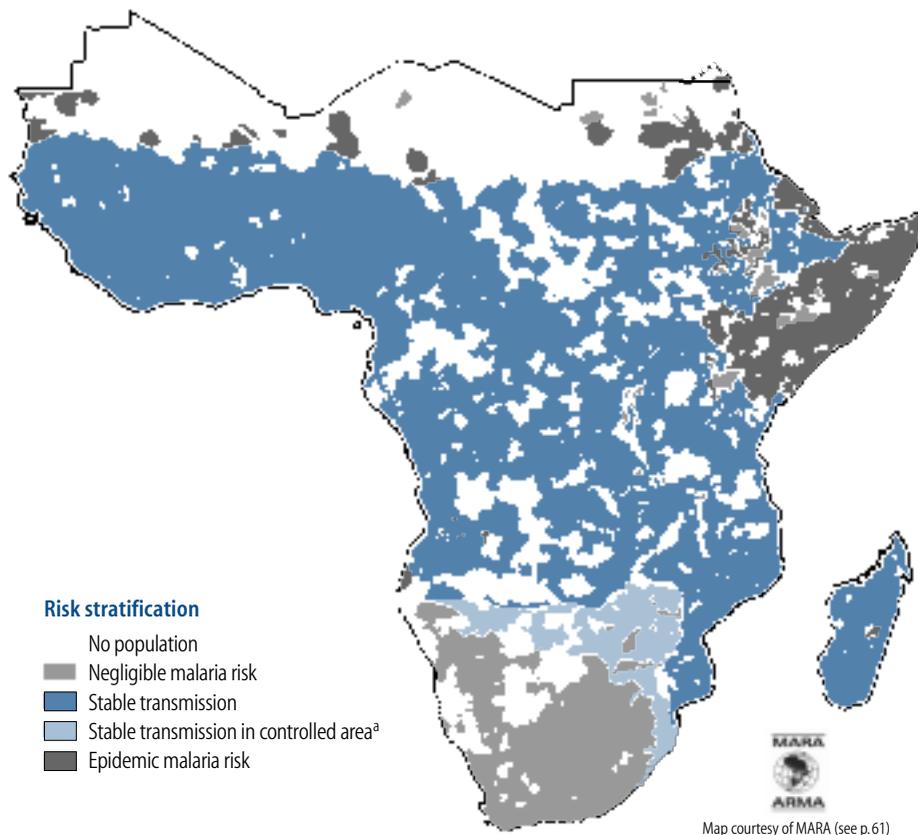
Government resources are also stretched in the provision of prevention and treatment services. Between 20% and 40% of outpatient visits and between 10% and 15% of hospital admissions in Africa are attributed to malaria, at an estimated cost of $1.10 per outpatient visit (Malawi) and $35 per admission (Kenya). In Rwanda nearly a fifth of the health budget was spent on malaria treatment in 1989. One estimate of the impact of malaria on national income in Africa *(2)* put the economic burden at 0.6–1.0% of gross domestic product (GDP); separate estimates for Kenya put the overall production loss at 2–6% of GDP, and at 1–5% for Nigeria *(3)*.

Recent research *(4)* suggests that the adverse economic impact of malaria in Africa is probably even greater than 1% of GDP. This figure is mainly made up of estimated productivity losses through premature mortality and spells of sickness. Further, malaria in schoolchildren is a major cause of absenteeism and probably reduces the effectiveness of their education. It is also thought to drive away potential development opportunities by making certain zones unsuitable for habitation, deterring international trade and foreign investment, and jeopardizing the development of sectors such as tourism. Economic development may also be retarded by reduced access to international flows of knowledge and technology because companies may be reluctant to send representatives to malarious countries. Malaria may thus be a cause, and not just a consequence, of underdevelopment.

THE DIVERSE AND CHANGING NATURE OF THE DISEASE

The endemicity of malaria is largely dependent on the type of mosquito, the parasite species, and the climate, which broadly determine the intensity and length of transmission. Figure 4.1 shows malaria risk levels across sub-Saharan Africa *(5)*. Of the four species of parasite that affect humans, *Plasmodium falciparum* is the most dangerous. It is also the parasite most common in Africa. Epidemic areas are subject to irregular rapid increases in incidence, usually related to the season and population movements, whereas in endemic areas malaria transmission occurs continuously over many successive years. Endemic malaria under very high intensities of transmission, commonly referred to as stable endemic malaria, primarily exists in tropical Africa (except in highland areas) and in Papua New Guinea. Moderate intensities of transmission with seasonal and year to year fluctuations, referred to as unstable endemic malaria, prevails in much of the rest of the malaria world, particularly in Asia and Central and South America. Epidemics of malaria can also occur over large parts of the Indian peninsula, Sri Lanka, parts of the Middle East, South-East Asia, north-west Africa and some countries in South America. In highly endemic areas, children and pregnant women are the most vulnerable to attack, as other adults acquire a degree of immunity through continued exposure. But in areas of less intense transmission

Figure 4.1 Malaria risk across sub-Saharan Africa according to population density and climate [a]

Risk stratification
- No population
- Negligible malaria risk
- Stable transmission
- Stable transmission in controlled area[a]
- Epidemic malaria risk

Map courtesy of MARA (see p.61)

[a] Modelled on estimates of population density and stable transmission (transmission and/or new clinical cases every year), according to combined temperature and rainfall. In addition, in southern Africa, the fact that there has been a successful control strategy for many years was also taken into account.

Source: **Snow RW et al.** *Mortality, morbidity and disability due to malaria: A review of the African literature.* Report prepared for the Epidemiology & Burden of Disease Programme and Roll Back Malaria. Geneva, World Health Organization, 1998.

and particularly in epidemic areas, most of the population is likely to be non-immune and all are at risk.

The toll in morbidity and mortality from malaria has been held in check by the widespread availability of cheap and effective antimalarial drugs. The greatest threat to the control of malaria in the near future is the loss of effectiveness of these drugs because of resistance. The potentially lethal malaria parasite, *P. falciparum*, has shown itself capable of developing resistance to nearly all the antimalarial drugs now used. Chloroquine, perhaps the best ever antimalarial drug, and certainly the most widely used, is now failing against falciparum malaria in most areas of the tropical world.

In some areas, such as parts of South-East Asia and South America, chloroquine is now completely ineffective against *P. falciparum* malaria. In many parts of India and Africa, its effectiveness is falling rapidly. Even *Plasmodium vivax* malaria, which has been consistently sensitive to chloroquine in the past, has now developed resistance in some parts of South-East Asia and Oceania.

For the treatment of falciparum malaria, the usual successor to chloroquine is a combination of pyrimethamine and a long acting sulphonamide (SP), which is also affordable

and well tolerated. Five countries in Africa (Botswana, Kenya, Malawi, South Africa and Swaziland) have now been forced to switch from chloroquine to SP as the first line antimalarial treatment. Unfortunately, in several of the areas where it has been deployed, notably South-East Asia and South America, *P. falciparum* has become widely SP-resistant.

Replacement drugs generally last only a few years before they too experience significant resistance. In some areas, such as Brazil and Thailand, only multi-drug therapies are now effective. Deciding when to change drugs is an extremely difficult decision, involving complex trade-offs between higher drug costs, immediate reductions in morbidity and mortality, reductions in the associated cost of treatment, and potential increases in resistance to replacement drugs, which could lead to higher morbidity and mortality in the future. Policymakers urgently need good data and practical advice to help them to choose the most appropriate drug regimen. Policies must be developed to balance the need for accessible treatment with the need to control drug use in order to reduce the growth in resistance.

Human beings play a crucial role in the epidemiology of malaria. Epidemics can result from population movement of non-immunes into malarious areas, either in search of temporary work, or into new frontier settlements, for example in jungle areas of South America, or as refugees, following natural disaster, war or civil unrest. Nchinda *(6)* cites armed conflict and migration as important causes of malaria resurgence in Africa. Economic activity and development can create conditions suitable for mosquito breeding through, for example, environmental changes such as deforestation, global warming and irrigation. Furthermore, previous patterns of antimalarial and insecticide use affect present levels of drug and insecticide resistance.

MALARIA CONTROL: PAST, PRESENT AND FUTURE

The nature of malaria and its impact on health is quite different in different places. So control operations must be specific to each location and need to take into account the epidemiological, economic, institutional and cultural settings. Patterns of promotive and preventive behaviour, and of treatment seeking, are influenced by levels of education and cultural beliefs. And the capacity to control both the disease and the growth of resistance depends on the quality and coverage of each country's general infrastructure and the state of its health system.

CONTROL STRATEGIES, 1950–1990S

Organized efforts to reduce the burden of malaria can be traced back to antiquity, and a historical perspective offers important insights into control strategies (see Box 4.2). In the postwar period several distinct shifts have occurred in global and national strategies to control malaria, reflecting changing attitudes to disease control in general and growing knowledge about malaria in particular.

The period from the late 1940s to the mid-1960s was a time of optimism. Following the discovery of DDT and the establishment of the World Health Organization, malaria eradication was identified as a priority. Time limited special-purpose campaigns, involving DDT spraying, chloroquine chemotherapy and active case surveillance, were expected to achieve global eradication in a matter of years. "This is the DDT era of malariology. For the first time it is economically feasible for nations, however undeveloped and whatever the climate, to banish malaria completely from their borders" wrote one authority in 1955 *(7)*. Cases of malaria fell dramatically in several countries, most notably in Sri Lanka (see Box 4.1), where they dropped from over one million cases a year to under twenty in 1963. But resistance

developed to DDT, and concerns about its safety emerged. External funding was scaled back, and public support for spraying wavered. By 1969, WHO had accepted that control programmes were indispensable in areas where eradication was impractical, such as sub-Saharan Africa (where eradication strategies were never attempted), and early optimism was giving way to disillusion.

International funding for malaria control and research shrank in the 1970s and 1980s, and the emphasis shifted to control strategies. But there were no clear guidelines, and many malaria programmes, set up originally as "one-off" eradication campaigns, were organizationally outside the rest of the health system. Resistance to chloroquine grew rapidly, first in Asia, subsequently in Africa. Major epidemics occurred in Brazil (1985–1989), India (1974–1977) and Turkey (1976–1978).

Although global malaria eradication was not achieved, gains were made, and important lessons were learned from the experience of the 1950s and 1960s. First, malaria was eradi-

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Box 4.2 Malaria control: lessons from the past

Organized efforts to reduce the burden of malaria are as old as human societies. From the time of the pre-Roman Etruscans to Napoleon, for example, efforts were made to drain the marshes surrounding Rome, whose "noisome smells" were believed to cause pestilence *(7)*. Hippocrates observed that "[where] there be rivers ... which drain off from the ground the stagnant water ... [the people] will be healthy and bright. But if there be no rivers, and the water that the people drink be marshy ... the physique of the people must show protruding bellies and enlarged spleens". Before the parasites were discovered and their life cycle characterized, malaria could only be associated with poor sanitation. Accordingly, therefore, most early efforts at malaria control focused on sanitation and land use strategy.

The expansion of colonial powers into the malarious tropics brought new urgency to European efforts to understand the etiology of malaria. Throughout the 19th century, a succession of colonial army officers, as well as scientists from Italy (which was malaria-endemic at the time), doggedly tracked the disease until its entire life cycle, etiology, and epidemiology had been elucidated in

detail. When Ronald Ross provided irrefutable empirical support for the mosquito theory, malaria intervention became aimed at reducing vector populations.

In addition to spurring the development of modern malariology, the increase of global traffic during the colonial period resulted in the importation of many infectious diseases to areas where they had not previously been endemic. Malaria, for example, was imported into Mauritius in 1866. Similar introductions of malaria occurred at the same time on Grand Comoros Island and Reunion Island. Malaria remained endemic in Mauritius and Reunion for a century before it was sustainably controlled.

By the time of the outbreak of the First World War, emerging success stories in Panama and southern Europe and unsuccessful attempts elsewhere spawned debates which would shape later international policies to control malaria transmission. Among these debates, the alternative conceptions of malaria as a social disease – to be solved by the elimination of poverty – and as an entomological and clinical problem which required proper scientific intervention strategy vied with each other for decades. Ultimately, the discovery of DDT's unprecedented insecticidal potential would infuse new

energy into vector-based approaches to malaria control.

The two World Wars, with their concomitant social upheaval, transformed anti-malaria efforts around the world. In the rural south of the United States and in southern Europe the prevalence of malaria had begun to decline. This was mainly attributable to the interplay between malaria transmission dynamics specific to these regions and to three important changes attendant on rapid economic growth.

• The drainage of swamps in order to establish new agricultural land had drastically reduced the indigenous anopheline populations of malaria endemic regions. Similarly, improved facilities in animal husbandry led to better separation of humans and livestock, and diverted the attention of more zoophilic vectors.

• Increased income provided at-risk individuals with the means to improve their health-seeking behaviour, including limiting their exposure to mosquitoes and seeking drug treatment. Many radical malaria treatment strategies aim not only to eliminate clinical symptoms of the disease but also to clear all parasites from the patient's blood. Similarly, increased national wealth allowed for the establishment of an

extensive health infrastructure, making primary clinical care easily accessible. Malaria was relatively easy to diagnose in these regions, where it was one of only a few vector-borne infectious diseases.

• The establishment of large cities created environments hostile to the spread of malaria.

Analysis of historical changes in malaria prevalence suggests a number of factors which help to determine the likelihood and sustainability of success in malaria control. Among these are geography, evolutionary history of flora and fauna, infrastructure, and land use. It is due to these factors, much more than to socioeconomic ones, that attempts to control or interrupt transmission of the disease have historically been most successful on islands, in temperate climates, or at high elevations. These lessons have important policy implications for malaria control; well-designed strategies ought to consider how such factors interact both locally and globally. Interventions must be critically assessed to ensure that they are suited to the geographical, economic and biological contexts in which they are carried out.

cated or controlled in ecological zones where infection was lower: in the many subtropical areas of southern Europe, the island settings of Mauritius and Singapore, in Hong Kong (China), and also in parts of Malaysia. Second, the importance of supportive health systems to malaria control efforts became clear. Sri Lanka came close to eradication in large part because of its well-organized and accessible health system.

By 1992, when a revised global malaria control strategy was approved by WHO's Member States at the World Health Assembly, there had been much re-thinking. Resistance had spread but new drugs and tools were becoming available. Malaria control was recognized to be an essential part of overall health development, and the importance of achieving sustainable progress was emphasized. National programmes were encouraged to focus on early diagnosis and prompt treatment, selective and sustainable prevention, early detection, containment and prevention of epidemics, and building local capacity to assess and manage the malaria situation. In Brazil, a control programme integrated within the health system rapidly expanded diagnostic and treatment facilities between 1992 and 1996 and achieved a substantial reduction in *P. falciparum* malaria transmission. Africa, the most affected region, took important initiatives (see Box 4.3). Mobilization of the research community was achieved with the launch of the Multilateral Initiative on Malaria in 1997.

CURRENT TECHNOLOGY FOR EFFECTIVE INTERVENTIONS

A wide range of effective tools for malaria prevention is at present available, though not always where most needed.

- Insecticide-treated nets have increasingly been used over the last 15 years as a method of preventing mosquito biting. Where nets are already widely used in the community, only a re-impregnation programme is required; but where net ownership is currently low, nets must also be distributed as part of the intervention. Large-scale use of insecticide-treated nets has been accompanied by substantial reductions in malaria incidence in China and Viet Nam. The use of treated bednets and curtains has led to reductions in child mortality ranging from 14% to 63% in African trials, but current implementation in Africa remains limited and achieving high retreatment rates of nets has proved very difficult. Nets are not a panacea.

Box 4.3 Malaria control in Africa

Malaria is the leading health problem in sub-Saharan Africa, where 74% of the population live in highly endemic areas and a further 18% live in epidemic areas. About 550 million people are at risk of malaria. There are about 270 million cases a year, with almost one million deaths; 5% of children are likely to die of malaria-related illness before they are five years old.

Malaria has spread into areas which previously had low transmission or none at all. For example, epidemics have occurred in recent years in some parts of eastern and southern Africa. This changing geographical distribution is influenced by population movements, as well as by global warming and deteriorating sanitation which make the environment more propitious for the breeding of mosquitos.

Countries in the African region have adopted a coordinated malaria control strategy which includes: the early detection, control or prevention of epidemics; early diagnosis of malaria cases, with prompt and effective treatment; preventive measures including vector control activities; and integration of activities into primary health care.

Over the past two years, capacity has been built in the areas of policy formulation, the planning and evaluation of malaria control programmes, and case management at all levels of the health system including the community. A review of health facilities in selected districts found that, in general, the quality of case management is improving. Uncomplicated cases of malaria were being correctly managed in 67–100% of health facilities and severe malaria in 28–100%. Preventive measures, such as indoor spraying, personal protection and the use of bednets, are being promoted.

Priorities for malaria control in Africa are now the strengthening of technical support to programmes, training, and enhanced operational research. Countries will be encouraged to build partnerships for the systematic implementation of the malaria control strategy, and communities will be encouraged to play a greater role.

Contributed by the WHO Regional Office for Africa.

- User-friendly packaging of drugs is a simple and cost-effective way to improve case management and compliance. Better regulation of drug vendors, which is also necessary, presents a bigger challenge.
- Access to early treatment of good quality remains a critical need. Effective treatment of African children could bring about an immediate reduction in the total disease burden. Chemoprophylaxis or presumptive treatment during pregnancy reduces the risk of malaria infection in all pregnant women and significantly increases the birth weight of babies born to women in their first pregnancy. Although WHO recommends that all pregnant women in malaria endemic areas receive regular prophylaxis, in practice less than 20% of women are effectively covered. For both women and children at risk from malaria, better functioning health systems have an important potential role.
- Using a stratified approach to residual house spraying and applying it in high-risk areas remains an important control activity in many countries. Larvicides or environmental management, such as drainage or control of water flow of rivers and other water bodies, can be used to destroy mosquito larvae, but only in areas where breeding sites are well defined.

For an intervention to be appropriate it must not only be effective but also cost-effective compared with alternative uses of scarce resources. The cost-effectiveness of each intervention will vary, depending on epidemiological factors (such as the length of transmission season), economic variables (such as local costs for staff, nets and drugs), and behavioural factors (such as adherence to drug regimens and retreatment rates for nets). The extent and quality of the existing health infrastructure is also a key factor in determining costs and cost-effectiveness. For example, the cost-effectiveness of insecticide-treated nets varies according to whether nets are available in the community, and the cost-effectiveness of presumptive treatment in pregnancy depends on whether there is already wide coverage of antenatal care.

Figure 4.2 shows the range of the cost per DALY averted by preventive strategies in poor areas of Africa with high levels of malaria transmission *(8)*. It also shows estimates (from different sources) of the cost per DALY averted from improved treatment interventions. It is possible to make rough comparisons with data for other health interventions, although the methodologies used may not be strictly comparable. For example, the cost-effectiveness of measles vaccination is between $2 and $17 per DALY averted, onchocerciasis vector control between $120 and $230, and the medical management of hypertension greater than $2000, converted to 1995 US$ *(9)*. The Brazilian national malaria control programme, with a mix of vector control and integrated early diagnosis and treatment, reduced the burden of malaria at an estimated cost of $65 per DALY averted. It has recently been argued that any interventions with a cost per DALY averted of less than $150 would count as cost-effective in low income countries. Compared with this threshold, all the malaria control interventions evaluated represent good value for money. These data are consistent with a cost per death avoided of between $750 and $2500. On this basis, the annual global cost of halving malaria deaths would be between $375 million and $1.25 billion.

Effective, low technology interventions can be used to improve the quality of case management, even in the presence of considerable drug resistance. The development of simple algorithms improves diagnosis, increased drug testing can help identify poor quality antimalarials, and training of providers in both the public and private sectors is needed to improve prescription practices. Providing simple instructions and pre-packaging drugs help to ensure that the correct course of treatment is taken, and the identification of severe cases

Figure 4.2 Comparative cost-effectiveness of selected malaria control interventions in a typical low income African country, US$, 1995
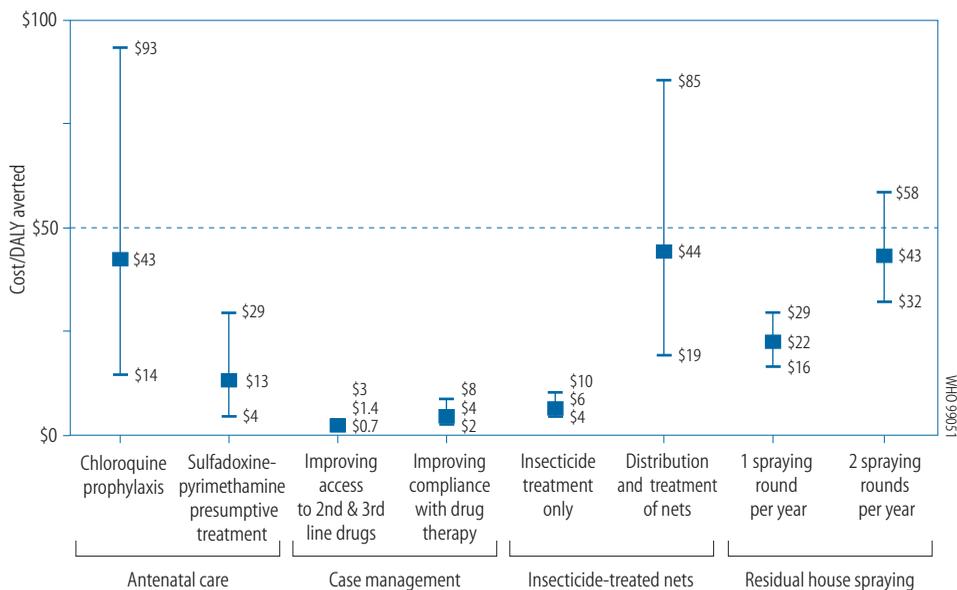
The following assumptions are made:
  – antenatal care: primigravidae only, 50% chloroquine RII/RIII resistance, 10% sulfadoxine-pyrimethamine RII/RIII resistance;
  – case management: gross costs, chloroquine as first line drug with 30% clinical failure;
  – insecticide-treated nets: one treatment of deltamethrin a year, no insecticide resistance;
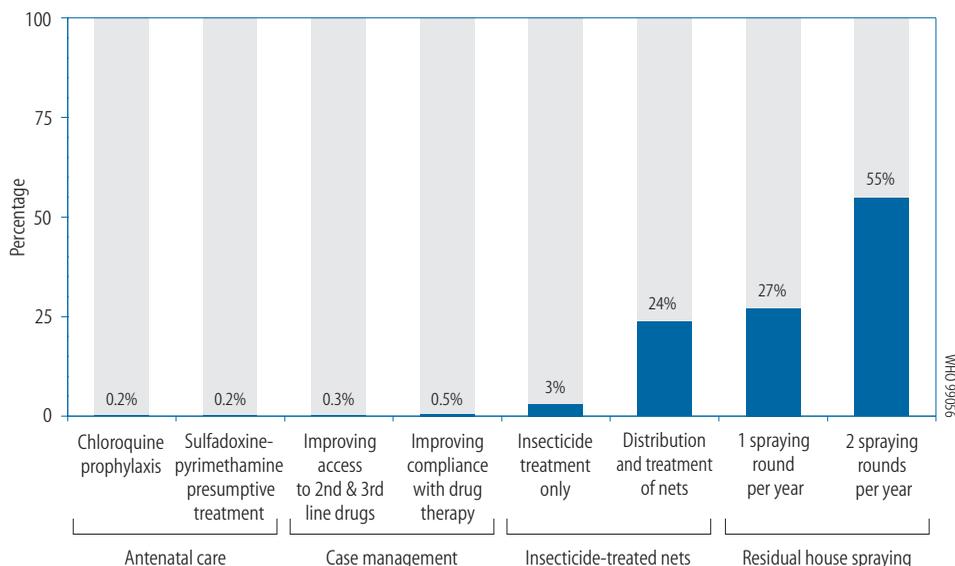 – residual house spraying: lambda-cyhalothrin, no insecticide resistance.
Adapted from: **Goodman CA, Coleman PG, Mills A.** *Economic analysis of malaria control in sub-Saharan Africa.* Report to Global Forum for Health Research. London, London School of Hygiene and Tropical Medicine (Health Economics and Financing Programme), 1998.

can be improved by community-wide health education. Where resistance is high, health outcomes can be improved by ensuring that treatment failures are recognized and treated with appropriate second line drugs. Although data are limited, several of these interventions are potentially highly cost-effective. For example, based on a situation of 30% clinical failure with chloroquine as first line drug, the cost per DALY averted of improving adherence through pre-packaging and education is likely to be under $8 in low income African countries, and improving the availability of second and third line drugs can cost less than $3 per DALY averted. Both interventions would be affordable to low income countries, requiring less than a 0.5% addition to the existing health sector budget.

An intervention can be cost-effective but also very expensive. Figure 4.3 shows the cost of implementing the different preventive and treatment interventions, as a percentage of the public sector health budget for a typical low income African country *(8)*. The results are striking. Whilst antenatal presumptive treatment and insecticide treatment of existing nets are both relatively inexpensive, distributing and treating nets on a national scale would require a budget increase of nearly 25%, and country-wide residual spraying would increase the budget by over 50%. These amounts are unaffordable to low income countries through government finance alone.

The focusing of public resources on a limited number of highly effective, low cost interventions will include preventive and promotive actions, and treatment of malaria. For example, the Integrated Management of Childhood Illness (IMCI) package is an initiative to improve the treatment of the most common childhood diseases and conditions. Malaria is one of five key conditions included in the strategy, along with acute respiratory infections,

**Figure 4.3 Comparative affordability of selected malaria control interventions: total cost of full
coverage as a percentage of a public sector health budget for a typical low income African country**

The following assumptions are made:
  – antenatal care: primigravidae only, 50% chloroquine RII/RIII resistance, 10% sulfadoxine-pyrimethamine RII/RIII resistance;
  – case management: gross costs, chloroquine as first line drug with 30% clinical failure;
  – insecticide-treated nets: one treatment of deltamethrin a year, no insecticide resistance;
  – residual house spraying: lambda-cyhalothrin, no insecticide resistance.
Adapted from: **Goodman CA, Coleman PG, Mills A.** *Economic analysis of malaria control in sub-Saharan Africa.* Report to Global Forum for
  Health Research. London, London School of Hygiene and Tropical Medicine (Health Economics and Financing Programme), 1998.

measles, diarrhoea and malnutrition. Integrated management involves the training of health
care staff and the provision of guidelines to help health care providers to recognize the
considerable overlap in the signs and symptoms of these common diseases, and to encour-
age prevention and appropriate treatment of children at home and in the health facility.

Preliminary estimates suggest that, in sub-Saharan Africa alone, IMCI could avert an-
nually over 400 000 deaths due to malaria in children. In addition, IMCI could avert a
further 350 000 childhood deaths from other causes in sub-Saharan Africa and perhaps five
times this number globally. In the *World development report 1993*, the World Bank estimated
the annual average cost of IMCI implementation at US$ 30–50 per DALY averted. This puts
IMCI in the middle range of the interventions presented in Figure 4.2. However, the abso-
lute impact of IMCI on disease burden would be considerably greater than that of most of
the interventions shown. WHO is conducting a multi-country evaluation of IMCI effec-
tiveness in order to provide more accurate figures.

Past experience has demonstrated that, although all of these strategies provide promis-
ing opportunities for improving the quality of care, their success will depend on integration
with, and development of, existing primary health care activities, and the strengthening of
health care services in general.

FUTURE CONTROL STRATEGIES AND RESEARCH NEEDS

The provision of prompt diagnosis and effective treatment should be a key component
of any control programme, but in reality disease management is often grossly inadequate.
This reflects a general weakness in the availability and quality of existing health systems.

A clear lesson from past experience of malaria control is that both prevention and treatment need to be delivered through a strong health system. Separate malaria organizations are not sustainable entities, and their effect has been to detract resources and attention from securing health system improvement and reform. Often, access to skilled care providers is impossible. Poor people face both price and time barriers in accessing health care. At first levels of care, providers may prescribe inappropriate drugs, patients may not comply with the recommended regimen, drugs are often ineffective because of resistance or poor quality, and patients with severe malaria are misdiagnosed or fail to get specialist care. Inadequate care results in unnecessary morbidity and mortality from malaria, and also encourages the development of drug resistance through the use of suboptimal doses.

Malaria control in the 21st century will be approached through strengthened health systems, working closely with local communities to identify and tackle the specific problems of the area. An impressive array of tools for preventive and effective treatment is already available. Big inroads can be made into malaria morbidity and mortality. The nine most endemic countries in the region of the Americas achieved a 60% reduction in malaria mortality between 1994 and 1997. Even with growing resistance, an estimated 20% reduction in child deaths in Africa could be achieved if health systems were funded, organized and managed to bring today's knowledge and techniques within the reach of whole populations. The state of the health system in most poor countries is itself a contributor to the scale of the malaria problem. Applying available knowledge is a prerequisite to future progress.

The Multilateral Initiative on Malaria in Africa (see Box 4.4) was created in 1997 to boost collaboration in malaria research to support strategies for control. The initiative aims to increase the funding for research on malaria (by one estimate currently just over 1% of the research funding level for HIV/AIDS) and bring together scientists, funding agencies, the pharmaceutical industry and government to identify common research priorities. Another joint public–private sector initiative is the Medicines for Malaria Venture (MMV) which aims to develop anti-malarial drugs and drug combinations and make them available in poor countries. Support for this venture is being solicited from foundations and other public sources as well as from the pharmaceutical industry.

Drugs, such as mefloquine, are now available, which are effective against multi-resistant falciparum malaria. But there are two problems; the first is that they are expensive and may cost 5–10 times as much per treatment as the drug they are succeeding. The second problem is that resistance can develop to these drugs, too. Artemisinin and its derivatives have proved the most rapidly acting and potent of all antimalarials. In large clinical trials these compounds have proved safe and effective, both in severe and uncomplicated malaria. The

Box 4.4 Multilateral Initiative on Malaria in Africa

The Multilateral Initiative on Malaria (MIM) was launched in Dakar, Senegal, in January 1997 when a number of institutions from both the public and private sectors joined forces to promote malaria research in Africa. In the context of this Initiative, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases is coordinating a Task Force on Malaria Research Capability Strengthening in Africa, which will focus on the needs of endemic countries and fund activities related to strengthening research capacities in malaria. A budget of about US$ 3 million a year has been raised, with contributions from several institutions to support research and capacity-building projects and training.

The Task Force has mobilized over 40 countries and 160 partners to submit proposals for review. Fifteen partnership projects involving 20 African and 5 European countries and the USA have so far been funded, and 14 research training grants have been approved in connection with the projects. The main research areas to be funded are antimalarial drug policy and chemotherapy, epidemiology, pathogenesis, vectors, and health systems and social science.

use of these drugs in combinations may provide an answer to the seemingly inexorable increase in resistance. Investigating this possibility is a major research priority. Combining artemisinin derivatives with mefloquine has been shown to halt the increase in mefloquine resistance on the western border of Thailand. Rational and appropriate use of these antimalarial drug combinations will require a concerted effort to educate medical personnel, dispensers, traditional healers and people living in endemic areas on the appropriate use of antimalarial drugs.

But malaria control is not exclusively a challenge of implementation. New knowledge, products and tools are urgently needed. In particular, new drugs are required. Investment in vaccine development now has a high probability of success. This and other discoveries in molecular genetics require political and financial guarantees to sustain their development into usable products, which the Multilateral Initiative on Malaria is working to secure. And careful economic and epidemiological research is needed to ensure that the most cost-effective mix of promotive, preventive and treatment actions is implemented to meet the needs of defined populations.

The versatility and adaptability of malaria pose a serious threat to successful control. This is particularly true in situations of war and social turmoil or of rapid environmental change. Over the last few years, several new and innovative products and strategies have become available and several others are at an advanced stage of development (see Box 4.5).

- Promising results have been achieved in early trials of suppositories containing the fast acting antimalarial, artesunate. Artesunate suppositories can be given to patients referred to hospital with severe malaria, who are unable to take oral medication. By allowing the rapid administration of an effective antimalarial their chance of survival both during transport and in hospital should be improved.

- New dipstick tests for diagnosing malaria are now on the market. The tests are quick and do not require sophisticated laboratory skills, equipment or an electricity supply. At over $1 per test, widescale use in Africa is unlikely to be affordable, but the tests could be cost-effective in improving the diagnostic accuracy in areas where expensive first line drugs such as mefloquine are used, or in the early confirmation of suspected epidemics.

- Combination therapies designed to slow the development of drug resistance are currently being tested. If two drugs are used together, the chance that a mutant will emerge

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Box 4.5 Malaria vaccine development

The development of an effective vaccine is the major breakthrough needed in malaria control. Even with much lower efficacy than other vaccines, a malaria vaccine is likely to be hugely cost-effective. Progress in understanding the immune mechanisms involved in conferring protection against malaria, and in identifying vaccine candidates and their genes, has been substantial. Vaccine development is now at a point of unprecedented opportunity, though it may take 7–15 years before an effective vaccine is ready.

Several different approaches to a malaria vaccine, using the latest advances in technology, are undergoing field testing on volunteers in Africa, Asia and the United States. The whole genome (the complete set of hereditary factors) of the malaria parasite is being sequenced.

Asexual blood stage vaccines, based on cocktails of antigens, have already been tested. Spf66, a synthetic peptide vaccine developed by Manuel Pattaroyo in the Instituto de Inmunología in Bogotá, Colombia, has been only partially effective in field tri-

als in South America, South-East Asia and Africa. Sophisticated biochemical methods are now being used to improve its potency.

A project taking advantage of DNA research is MuStDO 15.1 (multi-stage vaccine operation), a 15-gene malaria DNA vaccine designed to reduce morbidity and mortality in young children in sub-Saharan Africa. It is expected to enter clinical trials in the year 2000.

Already in field trials in the Gambia, a recombinant protein vaccine, RTS S, developed by SmithKline Biologicals, is designed to prevent the malaria

parasite infectious stage from entering or developing within human liver cells. Vaccines such as this will prevent the life-threatening consequences of malaria in non-immune individuals.

A different approach is a vaccine that prevents the transmission of the malaria parasite from an infected person to another. A transmission blocking vaccine is under development by scientists at the United States National Institutes of Health, in collaboration with WHO.

that is simultaneously resistant to both drugs is much lower than if the drugs are used alone. This strategy would increase drug costs in the short run, but could be highly beneficial if the useful life of available antimalarials is prolonged.

• For insecticide-treated nets, "dip-it-yourself" insecticide treatment kits are under development. These kits can be used in the home and should make retreatment more convenient. Social marketing strategies can be used to promote the use of treated nets.

Progress in the development of computer-based information systems allows geographical data to be combined with information on climate, environment, drug and pesticide resistance, population size and the location of health services. An example is MARA (Mapping Malaria Risk in Africa International Collaboration), an initiative to map malaria risk according to epidemiological type, which will provide vital information for assessing the disease burden and planning control. Information on the costs of malaria control, and how these vary by location and the scale of the intervention, is essential for the evaluation of both the cost-effectiveness and affordability of strategies. Operational research is necessary to devise ways to implement strategies which are sustainable and locally acceptable. Health services in general must be strengthened to provide a firm base for the delivery of malaria prevention and treatment, and new control strategies must be integrated within the national health care system.

A Global Programme to Roll Back Malaria

Several forces have combined to bring about the resurgence of malaria: civil conflict and large-scale human migrations, climatic and environmental change, inadequate and deteriorating health systems, and growing insecticide and drug resistance. For the following reasons, a new global initiative is timely.

• Malaria is a major problem. Although existing data are inadequate, it is clear that the level of the health burden of malaria, and its heavy incidence on the poorest populations, make it a powerful debilitating force.

• Tackling malaria is thus a major battle in the war against poverty. Malaria is a social and economic development issue, not just a health concern.

• Successful malaria control involves strengthening health systems. Weak health systems and uninvolved communities are part of the malaria problem. Because malaria is an acute condition with a rapid natural history, easy access to health care of good quality is vital in its management. Externally driven initiatives, by-passing local and national health systems, are neither sustainable nor supportive to malaria control and health development. Many countries have begun the process of reforming their health systems to improve performance. Malaria control, like the better management of all illnesses, needs to build on and support these changes. Through strengthened health systems, total malaria deaths could be halved for about $1 billion per year.

• A willingness to collaborate has been demonstrated. The Organization of African Unity, the World Bank and WHO's African Region have already planned a major African Malaria Initiative which is expected to spearhead Roll Back Malaria. The Multilateral Initiative on Malaria is under way, and a new alliance between public and private sectors in the form of the Medicines for Malaria Venture has been set up, aiming to improve the availability of effective antimalarials in poor countries.

Roll Back Malaria is different from previous efforts to fight malaria. It will work through new tools for controlling malaria, but also by strengthening health systems for sustainable health improvement. Roll Back Malaria's activities will be implemented through partnerships with international organizations, governments in endemic and non-endemic countries, academic institutions, the private sector and nongovernmental organizations (see Box 4.6). As agreed in October 1998, it will be supported by the united efforts of the four international agencies most concerned with malaria and its effects on health and the economy: UNICEF, the United Nations Development Programme, the World Bank and the World Health Organization.

Roll Back Malaria will act as a pathfinder, helping to set the direction and strategy for more integrated action in other priority areas such as tuberculosis control and safe motherhood. Greater reliance on partnerships in fighting malaria will inform WHO's approach to other major health challenges, and the development of effective and coordinated multi-partner action.

Though the disease burden from malaria is still very high, the situation has improved greatly since the beginning of the century. Trends in Africa are a conspicuous exception.

Since the beginning of the 1990s, a new international solidarity has arisen for renewal of the combat against malaria.

A major challenge is to optimize the use of available tools to deal with the disease, in coordination with all partners involved, through strengthened health systems; and to make a big step forward in research in the areas of vaccines and drugs.

Box 4.6 How Roll Back Malaria will operate

Governments and civil society in malaria-affected countries will take the lead in Roll Back Malaria (RBM) as a means to reduce poverty and mortality, and promote human development. UN system agencies will work with them: WHO, the World Bank, UNDP and UNICEF are committed partners. Other partners in the international initiative will include bilateral agencies, foundations, nongovernmental organizations, private sector entities (particularly research-based pharmaceutical companies) and the media. Partners will work together, at country level, towards common goals using agreed strategies and procedures. Usually the country's national authorities will direct the partnership.

Once a country has committed itself to the RBM initiative, it will undertake a situation analysis so partners can develop a strategy for intensified action against malaria. Partners will agree interventions for each location after examining information about the extent to which people prevent themselves from getting malaria; treat themselves when ill with malaria; and have access to good quality health care.

Partners will also consider health sector issues – particularly the institutional and financial context within which health care is being offered and used, both in the public and private sectors.

WHO has established a Cabinet project to help country RBM partnerships become fully effective. It supports them by:
• endorsing the technical content of strategies being pursued by partners;
• brokering technical and financial assistance for their implementation;

• encouraging partners to stick to their agreements;
• monitoring progress in rolling back malaria, within the context of health sector development.

To provide countries with the specialized technical support they need in tackling malaria, the project will sponsor a number of resource networks (initially a dozen), each concerned with a specific issue, such as avoiding resistance to antimalarial medication or insecticides. Networks will be made up of experts in the appropriate field – particularly from the relevant region. They will encourage collaboration between countries, will link malaria control teams with researchers and will optimize the use of local expertise in the management of malaria control activities. This will enable implementation plans to reflect an evidence-based response to local needs and

realities, in keeping with the Global Strategy for Malaria Control adopted in Amsterdam in 1992.

The project promotes effective investment in new medicines, vaccines and other tools to reduce malaria-related suffering through the Multilateral Research Initiative on Malaria and the public–private Medicines for Malaria Venture.

The project helps increase the level of international financial investment in countries' efforts to roll back malaria, through international advocacy with an emphasis on the current and potential investment outcomes – particularly among members of the global RBM partnership. The project will also ensure up-to-date aggregation and analysis of information on the global malaria situation.

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