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**A Decade of Progress in  
Malaria Policy  
and  
Program Development  
in Malawi:  
1984-1993**

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UNITED STATES AGENCY FOR INTERNATIONAL DEVELOPMENT  
and

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

Public Health Service  
Centers for Disease Control and Prevention  
International Health Program Office  
Atlanta, Georgia 30333



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## ABBREVIATIONS

ACSI-CCCD	Africa Child Survival Initiative-Combating Childhood Communicable Diseases
ANC	Antenatal clinic
AQ	Amodiaquine
ARI	Acute respiratory infection
CDC	Centers for Disease Control and Prevention
CQ	Chloroquine
EIR	Entomologic inoculation rate
GOM	Government of Malawi
HIS	Health information system
KAP	Knowledge, attitudes, and practices
LBW	Low birth weight
MMRP	Mangochi Malaria Research Project
MOH	Ministry of Health
MQ	Mefloquine
PHAM	Private Hospital Association of Malawi, subsequently known as Christian Hospital Association of Malawi (CHAM)
QECH	Queen Elizabeth Central Hospital
SP	Sulfadoxine-pyrimethamine
TBA	Traditional birth attendant
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
WHO	World Health Organization

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## PREFACE

Malaria infection and disease have exacted a heavy burden on sub-Saharan Africa, where the great majority of the world's malaria occurs. In this region, the health and economic burden of malaria surpasses that of all other diseases. In these endemic areas, children are at greatest risk and approximately 1.5 million children die each year of malaria. Exacerbating this problem for many years were inadequately funded, staffed, or organized malaria control programs throughout the region. In Malawi, the situation is no different. Malaria has been responsible for high levels of morbidity and mortality and has only recently benefitted from improved staffing and resources.

In 1981, the United States Agency for International Development (USAID) established the Africa Child Survival Initiative - Combating Childhood Communicable Diseases (ACSI-CCCD) Project, forming partnerships with the government of Malawi and 12 other sub-Saharan African countries to assist them in improving their capacity to reduce childhood illness and death caused by vaccine preventable illnesses, diarrheal diseases, and malaria. In Malawi, ACSI-CCCD efforts<sup>1</sup> and work supported by USAID/Malawi under the Promoting Health in Child Survival Project<sup>2</sup> emphasized the need for written policies and realistic plans for malaria control programs and assisted in developing health information systems and in conducting operational research to support these programmatic imperatives. Begun in 1992 as a 4-year project, the Health and Human Resources Analysis for Africa (HHRAA) Project was developed to continue efforts toward progress achieved through CCCD efforts. Its chief goals are to identify and fill information gaps to improve decisions, policies, and practices.

This document was written as part of the HHRAA Project to document Malawi's policy development process during the period 1984-1993. The focus of Malawi's activities was to define a locally appropriate malaria control policy and an effective malaria control program on the basis of knowledge obtained from evaluation of existing disease control activities and from relevant operational research. The document is intended as a case study describing the important link between gathering information, developing a talented group of nationals, and supporting appropriate decision making. The document is also intended as a tool for intercountry workshops and/or activities focusing on malaria policy. Malawi's progress in developing a malaria control policy and program could have important ramifications for other national disease control program efforts in Africa and for a broader regional formulation of malaria control policy.

Further malaria policy development in Malawi and in the region will require the commitment and efforts of many Ministry of Health officials, national policy makers, and malaria program managers in sub-Saharan Africa, donor organization personnel involved in program and policy development, and participants in intercountry activities of the USAID-World Health Organization/Africa Regional Office project. With their concerted efforts, lessons learned through Malawi's process of policy and program development as described in this document may help strengthen malaria control programs throughout Africa.

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<sup>1</sup> ACSI-CCCD efforts in Malawi were begun in 1984, scheduled to end in 1988, and continued until 1990 to complete the Mangochi Malaria Research Project.

<sup>2</sup> This project began in 1988 and continues through the time of publication, 1995.

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## EXECUTIVE SUMMARY

In Malawi, malaria infection and disease represent formidable problems. Malaria is the leading cause of illness and one of the major causes of death among children under the age of 5 years. During the decade from 1984 to 1993, the Government of Malawi (GOM), in collaboration with international agencies, systematically addressed its options for controlling malaria. During these years, Malawi defined a locally appropriate malaria control policy and began to develop an effective control program. This document describes the successes and limitations of efforts that resulted in what is generally considered important progress in malaria control policy and program development. Malawi's activities are presented as an example, a case study, of a country's efforts towards institutionalizing malaria control capacity at the national and local levels. This document details the process that Malawi employed — a process that used technical issues to engage key participants, a process that developed a national policy, two 5-year operational plans, treatment and prevention guidelines, and an infrastructure, and a process that developed the skills of people who became the resource base for sustained malaria control.

Malawi's malaria policy and program development process is presented in chronologic sequence: 1) the status of malaria and its control in Malawi in the early 1980s, 2) the period from 1984 to 1989, covering the initial development of a national malaria control policy and the first 5-year plan, and 3) the period from 1989 to 1993, covering the evaluation of the first 5 years and the development of a second 5-year plan. The process questioned "what is known" and "what needs to be known" to develop appropriate policies, plans, and programs. Consequently, the document provides examples of operational research used to establish a local information and knowledge base, which in turn led to policy and program development. The information and knowledge base is further described in terms of understanding the problems of malaria, the interventions necessary for its control, and the existing patient and health worker practices.

The success of Malawi's process can be measured in many ways: in the rational nature of the policy developed (a policy that established a national malaria control program responsible for guidance, with the implementation of malaria treatment and prevention integrated into general community, clinic, and hospital care), in landmarks reached (e.g., a Ministry of Health [MOH]-approved National Malaria Control Plan, health education materials developed, printed and distributed), and in its engagement of a broad base of people in health-related fields (policy makers, public health professionals, clinicians, traditional health workers, laboratorians, health educators, pharmacists). On the other hand, a decade is a relatively short time, and a malaria control program demands a long-term investment. Thus, while progress has been made, some areas require further attention and represent challenges to be addressed. Malaria program milestones and challenges are summarized below.

### MILESTONES

**Establishment of the National Malaria Control Program** In 1984, a National Malaria Control Committee was established to provide guidance and oversight to a National Malaria Control Program. A committee chairperson and committee members were selected from various parts of the health sector. The national program was established, and a program manager was identified and installed within the Department of Preventive Services.

**Elaboration of the National Malaria Control Policy and Plan** During the decade, a National Malaria Control Policy was drafted, revised, and approved by the MOH. Two 5-year plans (1985-1989, 1990-1994) were developed, approved, printed, and distributed with the involvement of clinicians, nurses, laboratorians, pharmacists, health educators, and other health professionals.

**Development of Malaria Treatment and Prevention Guidelines** Starting in 1984, malaria treatment and prevention guidelines were discussed, written, approved, printed, and distributed to all health facilities and clinicians (medical assistants, clinical officers, nurses, and physicians) in the country. The guidelines were developed after reviewing data collected from a variety of sources, including studies of drug efficacy, health worker behavior, and patient access to and utilization of health services. In response to new information and evolving patterns of drug efficacy, these guidelines were formally revised and reprinted on several occasions during the decade.

**Preparation of health education materials** From 1986 to 1988 and again in 1992 and 1993, health education materials for malaria control and prevention were discussed, developed, produced, and distributed to health facilities and to media throughout the country. The development of these materials was aided by information collected from local and national surveys.

**Formulation of malaria control policy based on locally acquired information** The development of national malaria control policies, national treatment and prevention guidelines, and materials for health education and other program components was based on information acquired within the country through operational research activities involving teams of Malawian researchers.

**Conduct of policy and coordination meetings** National and regional meetings were held to disseminate study results and to make policy and program decisions based on study findings.

**Development of a national program infrastructure** The National Program consists of a central office with two to three staff members. The program provides a technical base and program guidance, but the actual delivery of prevention measures and patient care services remains the responsibility of Division of Clinical Services, MOH. Consequently, the structure of the malaria program is horizontal, with disease control fully integrated and programmed in the clinics, health centers, and hospitals throughout the country.

Information gathering was accomplished through a link with the health information system for data review and trend assessment; sentinel sites were identified to examine specific questions. The program developed local research capacity through a network of trained staff in hospitals and clinics across the country. It also established mechanisms to monitor and re-examine parameters related to malaria disease prevention and control. When the national program undertook an internal and external evaluation of the program in 1989, the assessment benefited from the availability of data from its monitoring mechanisms.

**Contribution to the regional and international malaria control experience** The National Malaria Control Program has contributed directly to regional and international knowledge of malaria and its control through dissemination of research results and decisions made based on the results. Malawi's experience has had an impact on the malaria control policy of the World Health Organization (WHO) and disease control policies of its neighbors. Research projects conducted in Malawi have established operational standards in the field of malaria control (e.g., evaluation of in vivo drug efficacy, clinical criteria for examining severely ill patients).

**Involvement of partners in a multisectoral attack on malaria** The malaria control program has made important strides in health worker training and supervision, in consistent dialogue with the health education unit, and in full coordination with Clinical, Maternal and Child Health, and Primary Health Care Services in the MOH. Future efforts will rely on the strengthening of the coordination among these groups. The opportunity to engage private and estate clinics and practitioners, traditional healers, voluntary agencies, and other groups working in the health sector has not yet been fully exploited, the participation of these individuals and groups will come only with the availability of staff and resources.

**Development of personnel to conduct malaria control** The leaders of initial efforts in the malaria control program made a conscious effort to include people from a number of disciplines and to nurture their development. These efforts have persisted and continue to provide opportunities for young health workers to learn and participate as active members, not simply observers. This effort, as much or more than any other, will ensure the development of future leaders in malaria control in Malawi.

## CHALLENGES

The control of malaria in Malawi is a dynamic, ongoing process. The investments to date in identifying the challenges and effective interventions and in establishing a competent national staff have been essential initial steps. Continued investments in these areas will be required as the national attention moves to wider application of the control strategies, increased coverage, and greater access of the Malawian population to malaria control services. Distinct challenges remain that will require continued support and innovation to ensure that Malawi's malaria control program is effective.

**Ensuring adequate resources for malaria control** As with almost all disease control programs in developing countries, the malaria control program in Malawi has been faced with a limited MOH budget and continued requirements for donor assistance. While budget limitations have not jeopardized the control program to date, they have limited the planning capability and limited accomplishments by the national program. Recently available data from the economic evaluation of the cost of malaria to the country and its people provide important documentation of need, the MOH and donors must weigh this need against other needs within the health sector.

**Continued attention to develop the malaria control infrastructure** The small staff (both technical and administrative) and inadequate central resources (e.g., vehicles, basic equipment and supplies) for the National Malaria Control Program also limit the capabilities of the program to provide regional and district level guidance, supervision, training, and other services.

**Development of program management and administrative capacity** As is largely the case throughout the MOH, the staff of the malaria control program have little or no training or experience in management and supervision. This situation is unlikely to change except as improvements occur more widely within the MOH. Additional efforts to train potential leaders in these skills will need to be considered.

**Ensuring sustainability in malaria control programming** The National Malaria Control Program faces the continual question of adequate staff and resources to carry out its mission, as do other disease control programs. Recent efforts to train junior staff will undoubtedly foster the sustainability of the program, and continued informed advocacy by senior public health officials will remain essential to developing an effective malaria control program.

## MAJOR COMPONENTS OF MALAWI'S SUCCESS

Several elements of malaria control program development in Malawi should be highlighted. While these may not be models for other countries, they represent lessons for others to consider as they examine their own disease control policy development process.

**The study of technical issues served as an entry point for engagement and continued involvement of key participants.** This document describes the process of conducting operational research, examining study results, and making decisions based on locally collected information. While this process has been central to policy, planning, and program development, it has also engaged junior MOH staff (clinicians, nurses, public health staff, and other decision makers) and university staff and students. By obtaining skills needed to gather data and to apply results to policy and program issues, staff and students have strengthened their ability to contribute to the malaria control program.

The operational research activities engaged a variety of health care professionals, including physicians, who retain much of the decision-making power within the health sector. Physicians involved in these activities were encouraged to seek the relevance of their research to the malaria control program. Clinicians participated directly in evaluating determinants of antimalarial drug efficacy, in drug efficacy monitoring, and in examining diagnostic criteria for malaria and other diseases with overlapping symptoms (acute respiratory infection). From this engagement, clinicians further recognized the role and determinants of patient participation in effective malaria control. Subsequently, clinicians reviewed the knowledge, attitudes, and practices data along with health education and public health specialists to help focus malaria control programming efforts. Clinicians also recognized the need to evaluate the economic impact of malaria and disease control efforts in the context of people's economic limitations as an important step toward allocating resources and creating a program relevant to patient needs and means.

Technical issues that are highlighted in the document include

- Results of drug efficacy studies leading to changes in malaria treatment guidelines,
- Results of studies in malaria in pregnancy leading to changes in prevention guidelines,
- Knowledge, attitudes, and practices (KAP) survey results leading to health education material design,
- Results for an economic study focusing donor and MOH attention to malaria issues, and
- Studies of severe and complicated malaria providing information for improved treatment guidelines.

**Focused operational research supported malaria program development.** The contribution of operational research to program development has not always been adequately understood or supported. However, the experience in Malawi demonstrates the value of a partnership between program-relevant research and program development, in which focused scientific thinking supported and promoted program development.

In the evolution of the initial antimalarial drug efficacy studies and the subsequent studies to monitor drug efficacy, investigators in Malawi were faced with the question: how will we know when the antimalarial drug is no longer effective? This question was answered by defining the parameters of effectiveness (i.e., to resolve malaria-associated illness for a sufficient length of time to permit full recovery of the child including hematologic recovery) and then by developing a scientific study to examine whether the drug accomplished these requirements. Through this process, the information collected became directly relevant to the program's decision of when to change the first-line antimalarial drug.

Another example of the partnership of research and program development is the Mangochi Malaria Research Project (MMRP), conducted in Mangochi District. This project was developed to address a specific set of questions regarding whether or not a highly effective antimalarial drug used for prevention of malaria in pregnancy would lead to a reduction in the frequency of low birth weight in the population. This population-based research program led to an answer to this question of regional importance, and at the same time, results of the study led the Ministry of Health to seek an effective, affordable, and safe regimen that could be promoted for malaria prevention in pregnancy. In addition, important observations on malaria in pregnant women and their infants were made. The research fostered an ongoing collaboration between Malawian and U.S.-based malaria experts that continued to support systematic approaches to policy and program development.

While operational research served many important purposes in Malawi, the operational research described in Malawi is not meant to be a recipe for all such studies to be conducted in each malaria-endemic country in sub-Saharan Africa. In fact, it is hoped that information dissemination will play an increasing role so that relevant information from one country might be examined critically and adopted as appropriate to the local circumstances in another country in the same region. For example, a large-scale longitudinal study of malaria prevention in pregnancy, like the MMRP, need not be repeated in each country. Efforts are currently under way to develop simpler rapid assessment tools that can provide relevant information within a country. These tools should facilitate the adoption of the broad principles of malaria prevention in pregnancy and help tailor the program to local needs.

**The development of the malaria control infrastructure and management capacity is best addressed by training.** Although much remains to be done within Malawi in infrastructure and management development, the MOH has made a substantial effort to include staff in a variety of categories and levels, provide training, and offer young staff leadership opportunities. Malawi's malaria program has been built on the recognition that increasing management capacity requires both short- and long-term investment in training.

The ultimate sustainability of the malaria program, or any other disease control program, will be its ability to entice people to participate, to support them, to show progress, and to reward them for work well done. Malawi's program has contributed on these fronts, largely through the recognition by a few that these issues were important for the sustained nature of the effort. Clinical officers were brought into the decision making role, laboratorians were involved on a co-equal basis, and additional staff were trained in malaria control issues on their return from study abroad.

## **IMPLICATIONS FOR PROGRAM AND POLICY DEVELOPMENT ACTIVITIES IN SUB-SAHARAN AFRICAN COUNTRIES**

Malawi's experience accrued in the decade before the leadership of WHO and member countries adopted the Global Strategy for Malaria Control in Amsterdam in October 1992 (WHO 1993). The Global Strategy defines several control strategies, placing priority on the development of effective malaria case management and prevention services for all populations at risk for malaria infection and illness, both acute uncomplicated and severe. For effective case management, the Global Strategy recognizes that a national program must have a database to understand the current efficacy of antimalarials. Because of changing levels of antimalarial resistance, the strategy emphasizes that guidelines for case management cannot be rigid. The Global Strategy's focus on prevention highlights the importance of malaria prevention in pregnant women and the "personal protection" potentially provided by insecticide-impregnated bednets. The Global Strategy also emphasizes that a malaria control program capable

of providing effective treatment and preventive services will need a monitoring and evaluation mechanism, the results of which may prompt revision of malaria control plans and strategies. Finally, the global strategy acknowledges that for many countries limitations of resources and infrastructure will mean that locally relevant and affordable priorities will need to be established for malaria control.

The internal and international collaboration embraced by Malawi as it forged its National Malaria Control Program influenced the development of the Global Strategy and showed Malawi's position in the context of country-level programs. As noted in Box 9, the information generated from studies in Malawi that evaluated therapy efficacy and prevention effectiveness and set standards for assessing household practices and household and national expenditures has relevance, both within the region and globally.

Malawi's experience with malaria control comes at a time when the Global Strategy must define its relevance to local conditions. The translation of the Global Strategy to national and local programs is not dictated by formulas, but rather evolves from an assessment of malaria control priorities and of both financial and personnel resources available to the program. The iterative process of monitoring and evaluation (including operational research) that supports an official planning process embracing prompt and appropriate revisions in malaria control strategies is the core of program operations. This cyclical process forms the basis for effective and efficient malaria control, permitting adaptation to changing epidemiology and economic realities.

## **MALAWI'S NEXT STEPS**

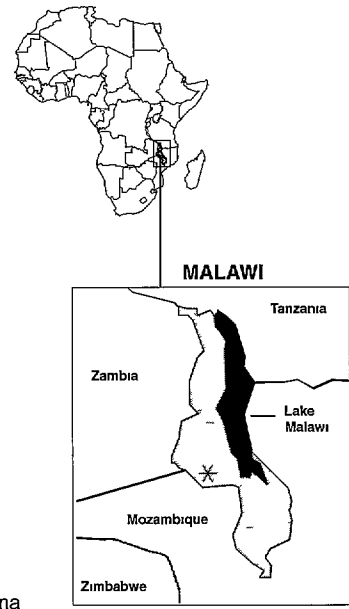
The challenges now facing Malawi's malaria control program are clear. Although the national malaria treatment guidelines have been disseminated nationally, efforts need to be focused on program support strategies that emphasize training, supervision, monitoring and evaluation through the health information system, administrative coordination, and operational research. The rate of expansion of program coverage will be dictated by resources and by the need to have a more systematic monitoring and evaluation component in the early phases to ensure that program process and impact are optimal.

The relationship between the Global Strategy and national malaria control programs must be dynamic. Local translation and adaptation of the guidance of the global strategy requires national initiative and perspective. In this context, the experience in Malawi has particular value. The national commitment to developing malaria control capacity will foster the opportunity to evolve concurrently with the renewed global commitment to strengthen malaria control.

# Introduction

Malawi, a densely populated country in sub-Saharan Africa, has numerous health challenges to address, including its high rate of infant and child mortality (Box 1) From 1984 to 1993, in collaboration with international agencies, the Government of Malawi (GOM) systematically addressed the adverse effects of malaria, the leading cause of illness and one of the major causes of death among children under the age of 5 years (Box 2, Figure 1) The focus of these activities was to define a locally appropriate malaria control policy and an effective malaria control program on the basis of knowledge obtained from evaluation of existing disease control activities and from focused operational research efforts Strong government commitment to developing the required programmatic infrastructure and the necessary database for rational policy development was critical to the Malawi program Malawi is a successful example of a productive partnership of research, policy development, and program implementation Malawi's progress in developing a malaria control policy and program has ramifications for other national program development efforts in Africa and for a broader regional formulation of malaria control policy

<b>Box 1 Malawi</b>	
Population (1992)	10.4 million
Population annual growth rate (1980-92)	4.3%
Population density (1992)	88 per sq km
Life expectancy (1992)	44 years
Crude birth rate (1992)	55 per 1000 population
Crude death rate (1992)	21 per 1000 population
GNP per capita (1991)	\$230
Under-5 mortality rate (1992)	226 per 1,000 live births
Infant mortality rate (1992)	143 per 1,000 live births



The figure consists of two maps. The top map is a map of the African continent with Malawi highlighted in a darker shade. A line connects this highlight to a larger, more detailed map of Malawi below. This detailed map shows Malawi's geographical context, including its borders with Tanzania to the north, Zambia to the west, Mozambique to the south, and Zimbabwe to the southwest. Lake Malawi is shown to the east of the country. A small star symbol is located in the southern part of Malawi on this map.

Sources: UNICEF's The State of The World's Children 1994; Encyclopedia Americana

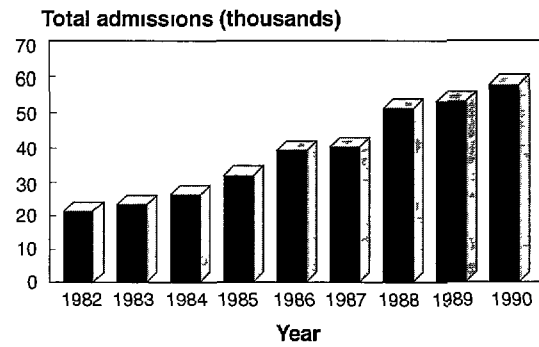
## Box 2 Malaria in Malawi

Parasites	<i>Plasmodium falciparum</i> (responsible for 80%-90% of malaria infections) <i>P. malariae</i> (responsible for 10%-20% of malaria infections), <i>P. ovale</i> (rare)
Vectors	<i>Anopheles gambiae</i> , <i>An. funestus</i>
Endemicity	Meso- to hyper endemic except in isolated higher altitude mountainous regions
Transmission	Perennial at lakeshore and lower Shire River valley, more seasonal on the plateau
Entomologic Inoculation Rate	Variable depending on region, estimates range between 15-50 infective bites per person per year

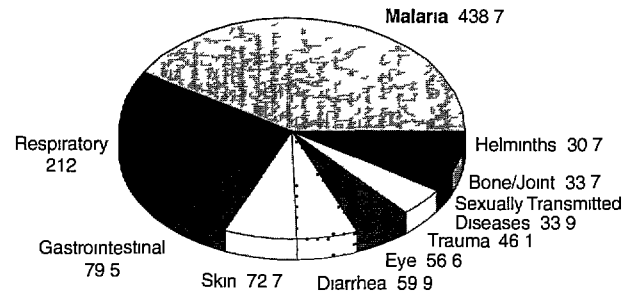


The health impact of malaria in Malawi

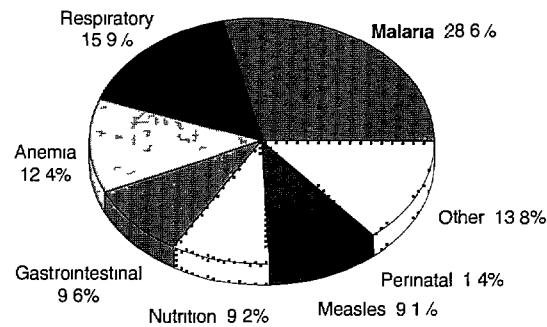
**Figure 1 Hospital admissions due to malaria, Malawi, 1982-1990**



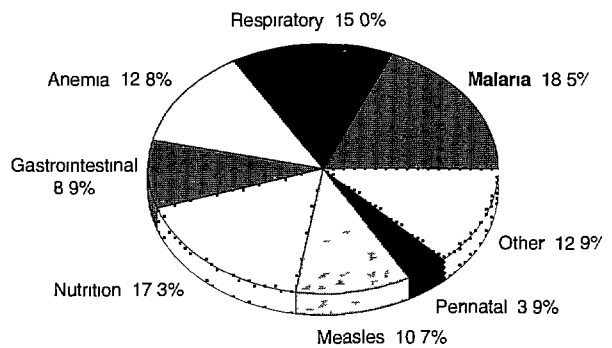
**Figure 2 Ten most common diagnoses made during outpatient visits, Malawi, 1990**



**Figure 3 Most common causes of hospitalization among children less than 5 years, Malawi, 1990**



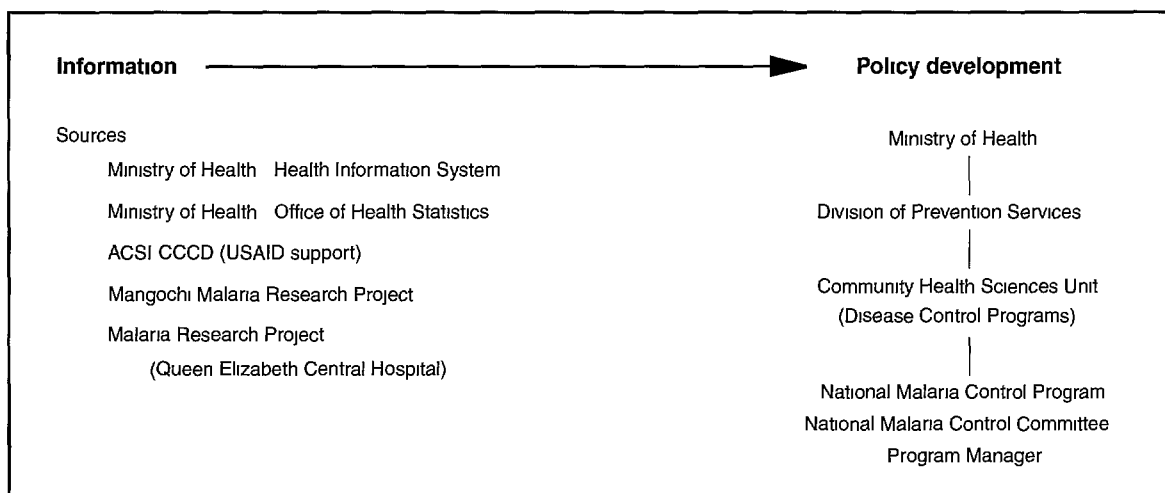
**Figure 4 Causes of hospital deaths among children less than 5 years, Malawi, 1990**



Source Malawi Ministry of Health Health Information System 1991

This document describes Malawi's development of a malaria control program, focusing on the program elements and infrastructure that evolved. Using basic epidemiologic methods, the Ministry of Health (MOH) defined the problem of malaria, effective interventions, and current malaria prevention and treatment practices (Figure 5). With this information, the MOH formulated malaria control policy and refocused its national malaria control program.

**Figure 5 Information sources for policy development**



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## CHAPTER I

# Status of Malaria Control Programs in the Region and in Malawi in the Early 1980s

In the early 1980s, much of Africa faced an increasingly serious public health crisis caused by malaria, yet it had little support, guidance, or experience in controlling malaria. The international effort to eradicate malaria in the 1950s and 1960s had failed to include most of Africa south of the Sahara (with the exception of Ethiopia, South Africa, and Zimbabwe) because the vector control interventions of the eradication program were not considered feasible in most of Africa. The intensity of malaria transmission and the limited health infrastructure available to support a program constituted impediments to the inclusion of most of this region. As of 1984, a limited number of African nations (Nigeria, Ethiopia, Zimbabwe, Swaziland, and South Africa) had approved written malaria policies and organized functioning malaria control programs.

Although health statistics in the vast majority of African nations indicated that malaria was one of the major causes of childhood mortality, few international organizations were committed to controlling malaria infection and disease, and consequently, few nations were prepared to embark on malaria control efforts. Looming on the horizon was the specter of decreasing effectiveness of chloroquine (CQ), the most widely used and available antimalarial drug in the region. Parasite resistance to this drug was first detected in East Africa in 1978 and was spreading into Central and West Africa. Drug resistance confirmed the prevailing attitude that malaria was not controllable in Africa; the erosion in the efficacy of presumably the only method of malaria control, mass distribution of CQ, caused many policy makers and national public health authorities to believe that malaria prevention efforts would have to wait, despite malaria's magnitude as a public health problem.

### I A Standard malaria treatment in Malawi in 1984

In 1984, Malawi, like many of its neighboring countries, had no organized malaria control program. The standard malaria treatment in its unwritten "policy" relied on chemoprophylactic and treatment doses of CQ for children under 5 years of age and pregnant women. Older children and other adults were not targeted for prophylaxis but received treatment with CQ when they presented with a febrile illness. However, the effectiveness of these regimens remained untested. Although the World Health Organization (WHO) had performed testing in 1978 and 1980 for resistance of the malaria parasite to CQ in Malawi, no surveillance system had been established to determine the presence or levels of CQ resistance on an ongoing basis, even after resistance had been detected in the neighboring countries of Kenya and Tanzania in 1978.

### I B The Africa Child Survival Initiative-Combating Childhood Communicable Diseases (ACSI-CCCD) and the Promoting Health in Child Survival Projects

In 1981, the United States Agency for International Development (USAID) established the ACSI-CCCD Project, forming partnerships with the government of Malawi and 12 other sub-Saharan African

### *Status of malaria control programs*

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countries to assist them in improving their capacity to reduce childhood illness and death caused by vaccine-preventable illnesses, diarrheal diseases, and malaria. ACSI-CCCD efforts (1984-1988 with continuation for the Mangochi Malaria Research Project until 1990) and work supported by USAID under the Promoting Health in Child Survival Project (1988-1993) emphasized the need for written policies and realistic plans for malaria control programs. These projects assisted in developing health information systems (HIS) and in conducting operational research to support national programs.

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## CHAPTER II

# Establishing the Organizational Structure and Developing the Policy for Malaria Control: 1984-1989

"Part II Establishing the organizational structure and developing the policy for malaria control 1984-1989 describes the significant malaria-related program and policy activities and the effect of Malawi's operational research agenda on malaria policy during this period. The studies that contributed to policy development and change are organized by the following categories: the problem of malaria, malaria interventions, and malaria treatment and prevention practices.<sup>3</sup>

### II A Summary of malaria program and policy accomplishments

During the years 1984 to 1989, Malawi established the basic elements of its malaria program: a malaria control committee, a committee coordinator, a national manager for the malaria control program, a policy (outlined in a 5-year plan and treatment guidelines), and health education materials (Figure 6). Policy and program activities were informed by research undertaken to assess the current malaria situation — disease prevalence, caretakers' knowledge, attitudes, and practices (KAP), treatment in the community and in the health facilities — and to evaluate treatment measures, including antimalarial drug efficacy (Figure 7).

**Figure 6 Malaria program and policy milestones 1984-1989**

1984	1985	1986	1987	1988	1989
Formed Malaria Control Committee					
Named malaria coordinator	Developed malaria control policy				
	Completed 1985-1989 Malaria Control Plan				
	Wrote <i>Guide for Management of Malaria</i>				
	Developed health education materials				
			Appointed national malaria control manager		
			Held national meeting		
					Held symposium on malaria control to disseminate new information
					Formally evaluated first years of malaria control program

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<sup>3</sup> A number of studies conducted during the years 1984 through 1993 contributed to the body of knowledge regarding malaria treatment and prevention but did not directly affect Malawi's policy. These studies are not described in this document.

**Figure 7 Studies affecting malaria policy development 1984-1989 \***

1984	1985	1986	1987	1988	1989
Malaria prevalence in facilities & community					
Evaluation of antimalarial resistance					
Clinical response to antimalarials					
	Community practices related to malaria control				
		Perinatal malaria prevention			
		Outpatient & inpatient treatment practices			
		Reevaluation of antimalarial drug resistance			
			Treatment of severe malaria		
			Malaria and infant mortality		
			Mangochi Malaria Research Project		

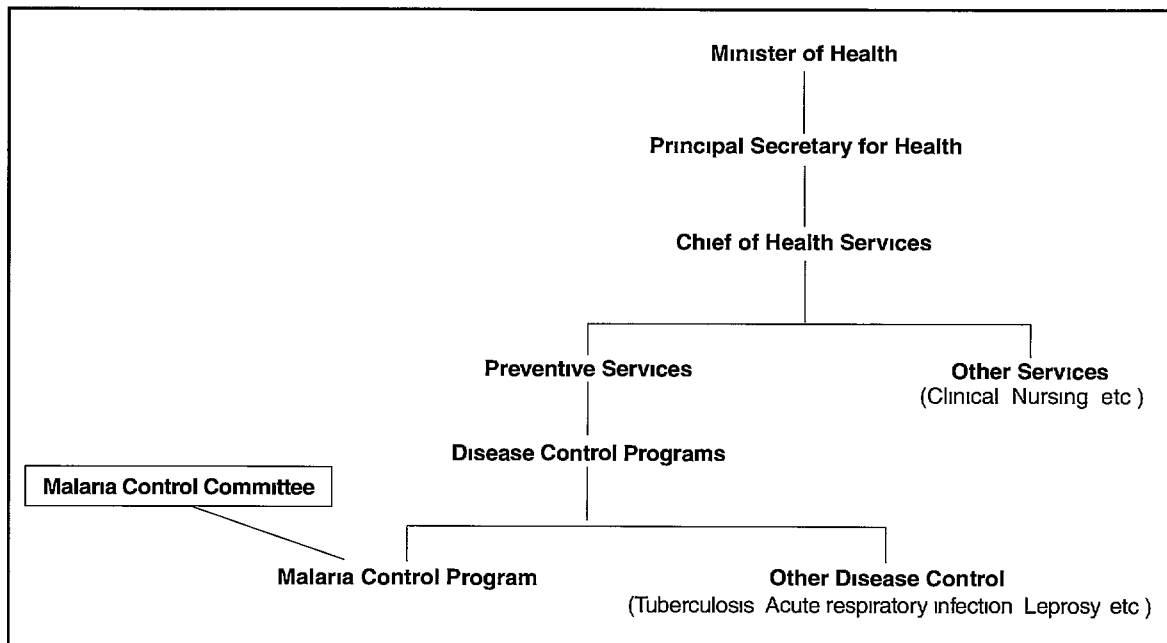
\*Time line indicates the year in which the studies were begun

## **II B Establishing the organizational structure**

In 1984, Malawi's National Malaria Control Committee was formed, and a chairman of the committee was named. Following the policy of the MOH in Malawi, malaria control activities were implemented at the three levels of health care delivery and were integrated within existing programs. At the national level, the malaria control committee developed plans for monitoring, evaluation, and research activities. The committee made policy recommendations that were then submitted to the MOH, GOM for approval. The position of program manager was established at the national level within the Department of Preventive Services (Figure 8), and the appointed manager worked with regional and district health officers to ensure that training, health education, and laboratory and pharmaceutical supplies were sufficient for program implementation. The logistics of drug supply remained in the hands of Central Medical Stores and district health officers.

The regional and district health officers supervised activities at their respective levels. Each year, regional and district plans were finalized at annual regional review meetings. Health service delivery and primary health care (PHC) workers were trained and supervised at both regional and district levels. Personnel from the national level participated in some of the training and supervisory activities when necessary. A manual for training health service delivery workers was developed and distributed to all districts in 1985. Since that time, the majority of health service delivery workers and other cadres in the community have received refresher training in malaria therapy. The training program involved committees and other groups that provided support for health education at the community level (e.g., district development committees, village health committees, area primary health care committees, community leaders). Traditional birth attendants (TBAs) and village volunteers were trained and supplied with drugs and training aids to provide malaria chemoprophylaxis and treatment at the community level.

Figure 8 Organizational structure of the Malawi Ministry of Health



### Box 3 Malawi's primary health care system.

A number of public and private organizations and individuals provide health services in Malawi: government missions and other nonprofit organizations, industry, private physicians, traditional healers and traditional birth attendants.

The Ministry of Health (MOH) sets health policy, provides direct health care, coordinates other health-related resources in the country and develops strategies and programs for disease control, disease prevention, patient care, and health care quality. The government provided nearly half of all health services, primarily curative services, until 1973 when a prevention-oriented Maternal and Child Health program was established with antenatal and under-5 clinics throughout the country. The MOH has begun to decentralize, giving more responsibility for planning and management to the three regions and 24 districts. The plan for basic health services calls for development of primary health care activities in primary health centers, subcenters, and health posts, as well as at the community level by selected community members. Health centers are considered essential to management and supervision of village-level primary health care activities.

After the government, the mission-sponsored health system, the Private Hospital Association of Malawi (PHAM) later called the Christian Hospital Association of Malawi is the largest provider of curative facilities and prevention programs. The Malawi government provides PHAM with approximately 40% of its revenues. PHAM operates 20 of the nation's 49 hospitals, it also operates a number of subsidiary facilities that provide outpatient services: 22 primary health centers, 100 health subcenters, and leprosy center and training school. A third provider of health care is industry (e.g. large tea estates and urban manufacturing firms) which provides outpatient health services to employees and their families.

In addition, the three principal urban areas of Lilongwe, Blantyre, and Zomba have a small number of private practitioners. In 1989, 41 Malawian medical practitioners registered under the Medical Council of Malawi, along with expatriate physicians and clinical officers, staffed public and private hospitals. Over 5,000 traditional healers, located in both urban and rural areas, provide curative treatment. About 400 of these belong to the Herbalists' Association, which maintains a link with the MOH.

## II C Developing the malaria control policy

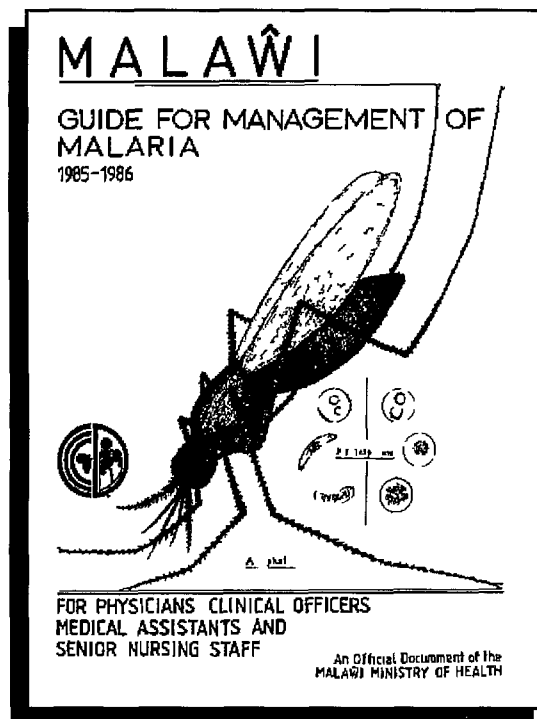
During the years 1984 to 1989, Malawi developed the policy documents needed for the newly organized control program and promoted malaria control through information dissemination

- In 1985, a malaria control policy was developed based on results of early field studies and was published in *The Malaria Control Plan 1985 1989* and the *Guide for Management of Malaria*

The Malaria Control Plan 1985-1989 outlined five basic malaria control strategies: presumptive treatment of fevers in children and adults with 25 mg base/kg of CQ, continuous monitoring of antimalarial efficacy, selective antimalarial chemoprophylaxis (for pregnant women, immunosuppressed patients, children with recurring febrile convulsions or sickle cell disease), vector control (limited to major urban areas), and health education

The *Guide for Management of Malaria* was developed in 1985 and distributed to physicians, clinical officers, medical assistants, and senior nursing staff (Figure 9). The guide explained the results of in vivo testing and recommended antimalarial drugs and their correct dosages. The guide also recommended regular monitoring of in vivo clinical response to CQ, amodiaquine (AQ), sulfadoxine-pyrimethamine (SP), and quinine. The guide was updated in 1986, and two recommendations contained in the 1985 guidelines were dropped from the 1986 guidelines. Aspirin was no longer recommended as adjunct treatment for acute episodes in children because of concern over Reye's syndrome, and AQ was not recommended for chemoprophylactic use, although it was still considered an effective second-line antimalarial treatment.

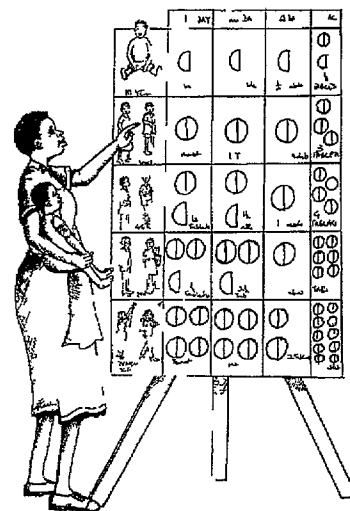
Figure 9 Cover of Malawi's 1985 treatment guidelines





- Realizing the need to disseminate information to both caretakers and health facilities, the committee developed health education materials. In 1985, a dose-for-age chart was developed and widely distributed. The chart (Figure 10) showed the correct number of CQ tablets to take based on a person's age, its use of pictures helped convey its meaning to the large numbers of people attending clinics who could not read. In 1989, Healthcom, a U S -based health organization, assisted the MOH in developing a wide variety of health education materials focusing on malaria treatment and prevention.

**Figure 10 Dose-for-age chart, Malawi**



Yanganani pa chithunzi ichi ndandomeka  
ya kaperekedwe ka kototakwini kuti  
mudziwe m mene mungam patsire  
mankhwa mwana

- In 1987, a national manager for malaria control was appointed, and the first national meeting to discuss malaria was held in Salima. Officials from the MOH and from nongovernmental organizations met and outlined a plan to implement malaria control efforts, with emphasis on strengthening delivery at the community level. The responsibilities and interrelationship of each level of the government in conducting the malaria control program were outlined.
- In February and March, 1989, the Medical Association of Malawi hosted a symposium on malaria control in Africa. Participants included clinical officers and physicians from across the country, international, regional, and national experts, and government officials. Malawi's guidelines were presented and discussed. The symposium served two major purposes: to widely disseminate information about study findings to clinical officers and physicians and to heighten the MOH's awareness of the problem of malaria and the new opportunities for control efforts.
- In June, 1989, a joint team of more than 20 officials from the MOH and nongovernmental organizations in Malawi, United Nations Children's Fund (UNICEF), USAID, and WHO conducted a formal review of the National Malaria Program. Findings of this evaluation are discussed in Part III.

## **II D Information gathered and its effect on malaria policy**

### **II D 1 Operational research agenda 1984-1989**

The National Malaria Control Committee developed an annual plan for operational research activities. To develop an effective malaria policy and program, the committee needed information in the following areas: current information on the extent of the problem of malaria, the efficacy of malaria interventions, and optimal delivery methods and effectiveness of malaria treatment and prevention practices.

*The problem of malaria* A WHO mission in 1973 had documented high infection rates among children under 5 years of age, but Malawi needed current information on malaria prevalence among those targeted for malaria control efforts. Fever rates, *P falciparum* infection rates, and severe malaria disease rates in the community and in health facilities were needed to fully understand the extent of morbidity in potential target populations and to understand the current burden of malaria on the home and health facilities. To compare the burden of malaria with that of other childhood diseases, information was needed on overall, site-specific (home versus health facility), and cause-specific mortality.

*Malaria interventions* Standard malaria treatment and prevention in 1984 were based on WHO recommendations for malaria control in Africa: treatment of acute malaria (febrile illness) with CQ for all persons and chemoprophylaxis with CQ for children under 5 years of age and pregnant women. However, the efficacy of these interventions was untested. Although *in vivo* and *in vitro* testing in 1978 and 1979 had shown that CQ was effective in a dose of 25 mg base/kg, clinicians from hospitals throughout the country during the 1982 and 1983 malaria seasons had begun to report an increase in breakthroughs of clinical malaria among children enrolled in CQ (5 mg base/kg weekly) chemoprophylaxis programs. In addition, CQ treatment failures of slide-confirmed malaria were observed among children and adults. At the same time, reports appeared in the international literature about expatriates living or having lived in Malawi at some time during 1983 who had chloroquine-resistant malaria infections (Fogh et al 1984, Overbosch et al 1984). It was apparent that the efficacy of CQ in clearing parasitemia as well as malaria symptoms in children needed further examination. Because results from new studies began to show poor efficacy of CQ in therapeutic doses of 25 mg base/kg, it was unclear whether CQ could be beneficial when used in a program of low-dose chemoprophylaxis for pregnant women, and testing of interventions was initiated for this group. Questions remained about safe and effective interventions for severe malaria, and studies were carried out to clarify optimal treatment for this manifestation of malaria disease.

*Malaria practices* With the knowledge that an effective malaria program requires both community (caretaker) participation and health facility delivery, current knowledge of how caretakers and pregnant women treated malaria and of how health workers provided malaria treatment needed to be evaluated so that appropriate actions could be taken to improve care in the community and, if needed, in health facilities.

The next three sections review the results of studies conducted to evaluate the problem, the interventions, and the practices. A brief description of the question or questions to be answered by the study and study findings is followed by a summary of the effect of each study on Malawi's malaria policy.

## II D 2 Studies of the problem of malaria

### II D 2 a Prevalence of malaria among children in health facilities and in the community

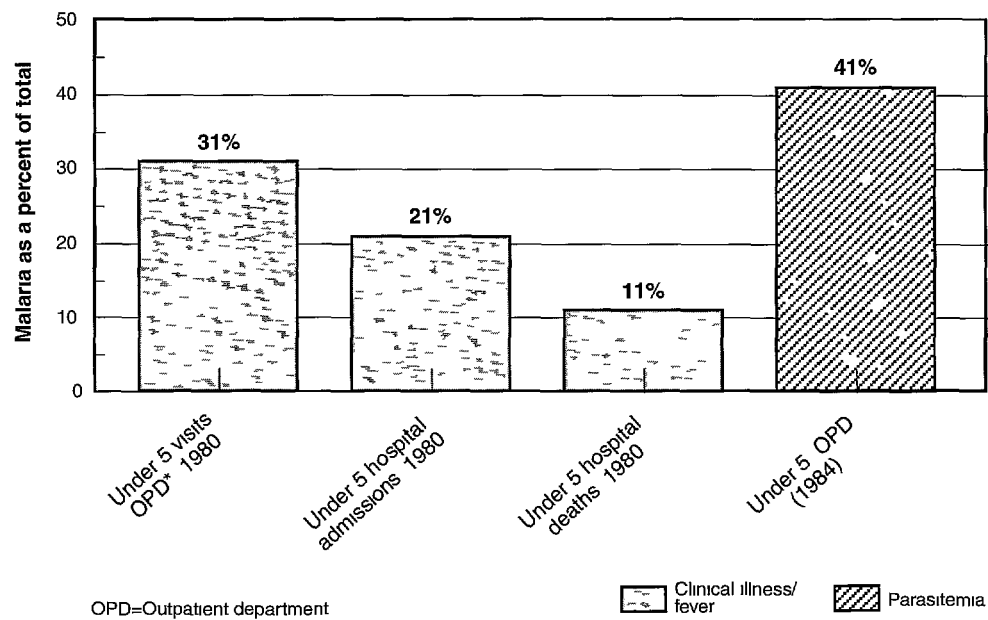
#### The question

To determine the extent of the problem of malaria in children, the number of cases of *P falciparum* in health facilities was assessed through routine outpatient and inpatient reporting systems, the prevalence of malaria in the community was established by community surveys

#### Study findings

*The extent of malaria in health facilities* Data obtained from the routine outpatient and inpatient reporting systems between 1980 and 1986<sup>4</sup> showed that malaria, diagnosed on the basis of clinical signs and documented parasitemia was a problem of substantial magnitude in health facilities particularly among children under the age of 5 years (Figure 11)

**Figure 11 Extent of clinical malaria and parasitemia among children less than 5 years of age, health facilities, Malawi, 1980-1984**



Among children under the age of 5 admitted to hospitals cerebral malaria signs accompanied malaria in 17% of all malaria admissions, and anemia accounted for progressively more admissions from 5% in 1980 to 14% in 1986. Approximately 41% of children visiting health facilities and clinics were parasitemic (Figure 11). Most (92%) of the infections among the children under 5 were of parasite density less than 2000 parasites/mm<sup>3</sup> and asymptomatic.

<sup>4</sup> Reports of malaria from outpatient facilities were based on presumptive diagnosis usually fever without signs or symptoms associated with other diseases. Reports of inpatient malaria were based on thick smear results though at times because not all hospitals had functioning microscopes the inpatient diagnosis was presumptive. Anemia in children under 5 years who had no parasites on a thick smear was not reported as malaria although anemia was often thought to be a direct result of malaria infection.

*Fever and parasite prevalence in the community* Children experienced a high number of febrile episodes regardless of season and location with an average of 13 episodes per child per year in the dry season nationwide and 17 episodes per child per year at the lakeshore. A great number of well children under 5 years were parasitemic. At the lakeshore rates of parasitemia ranged from 64% in the dry season to 78% in the wet season. Schoolchildren aged 6 to 15 years had much lower rates of falciparum infection only 29% were parasitemic and none were febrile.

### **Impact on policy**

These early prevalence surveys provided support for the malaria policy's targeting children under the age of 5 years as an at risk group. The magnitude of the problem provided justification for the intense focus on malaria by the GOM within the CCCD project. The finding that anemia was increasing caused concern and provided additional evidence that CQ resistance might be increasing. This potential increase in CQ resistance emphasized the need for ongoing evaluation of the efficacy of CQ and of its effectiveness when used in a regimen of prompt treatment with a full dose.

## **II D 2 b Perinatal malaria**

### **The questions**

Although chloroquine resistant *P. falciparum* parasites were widespread in Malawi (Khoromana et al 1986) CQ remained the first-line drug because of its ability to reduce parasite densities and clinical illness. As a consequence the existing policy of CQ prophylaxis for all pregnant women was continued in antenatal clinics (ANCs). However the efficacy and effectiveness of CQ prophylaxis among pregnant women had not been examined and there was serious concern that if CQ was not fully efficacious at therapeutic doses (25 mg base/kg over 3 days) it might offer little benefit when used as low dose prophylaxis (approximately 5 mg base/kg weekly). On the basis of these concerns, a series of studies was conducted to examine the problem of malaria in pregnant women, effective interventions, and a means of improving delivery of the interventions. Studies were conducted to examine the prevalence of infection, risk groups, consequences of infection, the efficacy of the recommended CQ chemoprophylaxis (see II D 2 b) and the compliance of pregnant women to the regimen<sup>5</sup> (see II D 3 c).

### **Study findings**

*Prevalence of parasitemia in pregnancy* During a 2.5-year period at the lakeshore site of Mangochi District 44.5% of pregnant women were parasitemic at the time of their first ANC visit. Women in their first or second pregnancies, women pregnant during the high transmission season, and those not using any prophylaxis were more likely to be parasitemic than their counterparts. Reported recent fever was not a good predictor of which women were parasitemic, and clinical illness was not a prominent feature associated with malaria infection.

*Frequency of low birth weight (LBW)* A mother's malaria infection may cause her baby to be born with LBW (<2500 grams). Its frequency was high in the population: 16.6% of babies were LBW. Low birth weight was observed in 28% of first-borns, 16% of second-borns, and 10.12% of babies of higher birth order. LBW was the strongest risk factor for infant mortality, causing a 4-fold increased risk of mortality in LBW babies compared with those of normal birth weight.

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<sup>5</sup> The Mangochi Malaria Research Project, a 3-year longitudinal study, was undertaken to determine the effect of malaria prevention with an efficacious antimalarial on placental malaria infection and low birth weight. Its design and methods have been discussed in detail elsewhere (Steketee et al 1993d).

### **Impact on policy**

These findings clarified the extent of the problem of malaria among pregnant women. A high prevalence of infection was seen in pregnant women, particularly those in their first and second pregnancies. A high frequency of LBW was observed, particularly in first- and second-born infants. This led to consideration of a change in the national policy to target malaria prevention to women in their first and second pregnancies only. In addition, the finding that fever was not a good predictor of parasitemia reconfirmed that the intervention needed to be provided to pregnant women without regard to clinical findings such as fever.

## **II D 2 c Malaria and infant mortality**

### **The questions**

To understand more completely the impact of malaria in infancy and to improve malaria treatment strategies for young children, the committee needed additional information on overall and cause specific infant mortality, including an estimate of what proportion of infants were dying outside health care facilities. From 1987 to 1989, population based information on infant mortality was collected in the Mangochi Malana Research Project (MMRP); this information was compared with health facility data from the national HIS.

### **Study findings**

*Infant mortality* The overall infant mortality rate in Mangochi District (a rural area) was 163 per 1 000 live births. The neonatal (birth through day 28) and postneonatal (day 28 through day 364) mortality rates were 49 and 111 deaths per 1 000 live births, respectively.

*Cause of death* The specific cause of death in the neonatal period was frequently not able to be determined. Among reported deaths with specific symptoms, illness consistent with sepsis/tetanus was most frequent (19%). In the postneonatal period, symptoms consistent with malaria were the second most commonly reported cause of death (19%), only symptoms consistent with gastroenteritis (39%) were reported more frequently.

*Duration of illness* The duration of the illness prior to death was generally brief. Information obtained from the parent or caretaker of the ill child demonstrated that 70% of the deaths occurred within 7 days of the onset of illness, 38% died within the first 3 days. Only 6% of deaths occurred after a reported illness of more than 1 month.

*Location of death* Nearly two thirds of infant deaths were reported to occur at home, the rest occurred at a health care facility. Of the neonates who died, 53% died at home, this proportion increased to 70% among infants in the postneonatal period. Almost two-thirds of reported deaths due to fever/malaria, respiratory disease, gastroenteritis, measles, and sepsis occurred outside health care facilities.

### **Impact on policy**

Information from the MMRP and the HIS helped define the full impact of the problem of malaria. These data documented the high infant mortality occurring in rural Malawi and provided an estimate of the proportion of this mortality attributable to malaria. In addition, the striking findings that most deaths in infancy occur very rapidly after the onset of illness and that for every death occurring at a health facility, two additional deaths occur in the community, highlight the importance of developing malaria policy focused on addressing the need for prompt recognition and proper treatment of malaria in young children in the community setting.

These data were considered in the formulation of 1990 National Plan for Malaria Control. These revised strategies to improve malaria control reflected the need to ensure prompt recognition and treatment of malaria in

very young children at the community level. In particular, three approaches were articulated to address this need. First, to ensure the availability of the appropriate antimalarials at all levels of health care, the need to strengthen the antimalarial drug supply and distribution system throughout Malawi, particularly at the community level, was recognized. Second, the need to train additional community volunteers and village health workers as well as health service delivery personnel in the effective management of malaria was identified. Finally, the need for increased efforts at education to inform the public, particularly mothers or caretakers, about recognition and effective treatment of malaria was acknowledged.

## **II D 3 Studies of malaria interventions**

### **II D 3 a Parasitologic and clinical response to antimalarial drugs**

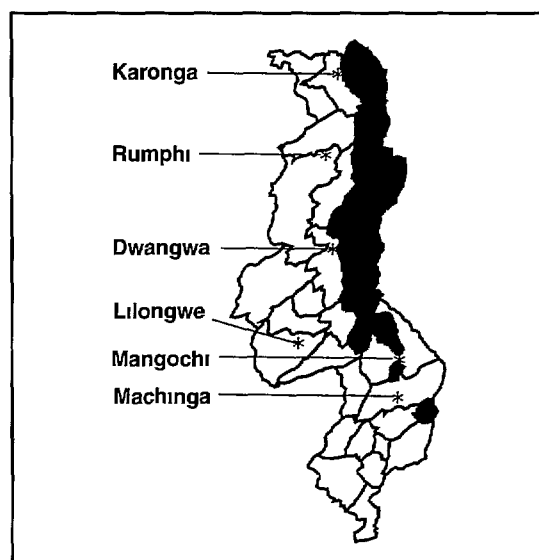
#### ***The questions***

The Ministry's concern about emerging CQ resistance and the lack of assessment of the effectiveness of the current malaria policy led in early 1984 to a plan to evaluate systematically the current malaria control policies and activities. The plan included selection of six sentinel sites for intensified malaria study, selection and training of malaria surveillance teams, and a series of field studies. The main focus of these studies was to evaluate the parasitologic and clinical response to antimalarial drugs.

#### ***The methodology***

*Sentinel surveillance sites* Six sentinel sites, two in each administrative region, were selected as sites at which to evaluate parasitologic and clinical response to antimalarials (Figure 12). Three of the sites were near the lakeshore at altitudes of 200–300 meters, where year-round malaria transmission is intense; three were at altitudes of 1 000–1 500 meters, where transmission decreases during the cold and dry winter months. Each site had an inpatient facility with electricity, ample space in the outpatient facility, and a laboratory in which the malaria surveillance teams could work.

**Figure 12 Map of sentinel surveillance sites, Malawi**



**Malaria surveillance teams** In 1984 three regional malaria surveillance teams of three members each were formed. Each team was composed of a clinical officer (a health worker with advanced training in clinical diagnosis and minor surgery), a laboratory technician, and a laboratory assistant. Initial training of the surveillance teams consisted of a review of malaria parasitology and epidemiology, patterns of resistance to antimalarial drugs, and methods of in vivo testing for resistance (Box 5). Special emphasis was placed on preparing thick smears, staining them with Giemsa, and identifying and quantifying parasites. Training was divided between the classroom, the laboratory, and the field. The initial CQ resistance testing at one sentinel site was included as the field training activity.

#### Box 4 Measuring drug resistance

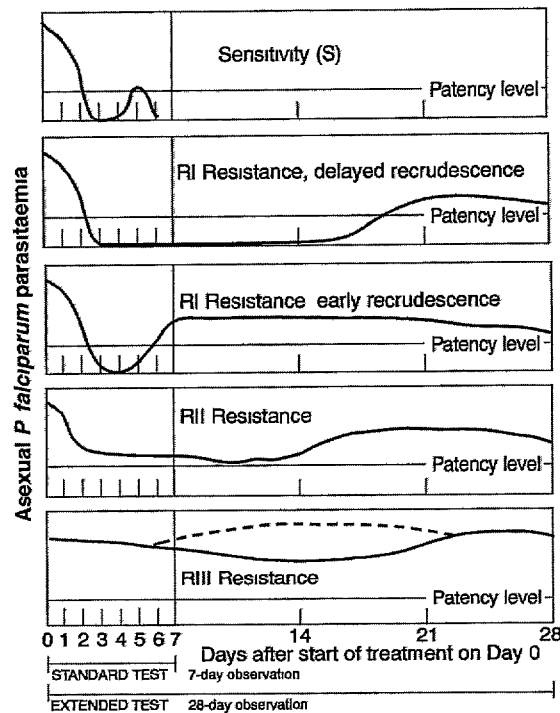
##### Recognizing drug resistance

Drug resistance in malaria parasites is generally first noted by clinicians when patients fail to respond to the standard treatment regimen. For chloroquine, deterioration in drug efficacy is a gradual process. Initially, only a few patients are affected. They may improve symptomatically, but parasitemia reappears within 3–4 weeks (RI, see chart below). In time, a substantial proportion of the patient population will be infected with chloroquine-resistant *P. falciparum*, and the resistance may be such that parasitemia does not diminish at all after treatment (RIII, see below).

##### Measuring drug resistance

The development of drug resistance in a population of malaria parasites can be measured in vivo (by noting inadequate responses to properly administered treatment) or in vitro (by measuring the effect of various concentrations of the drug on the growth of malaria parasites in culture). For operational purposes, in vivo testing is most useful.

##### Resistance Levels



Reproduced by permission of the World Health Organization, Geneva, from Technical Report Series No. 529, Chemotherapy of Malaria and Resistance to Antimalarials, 1973.

**Box 5 Methodology for in vivo testing**

A modified version of the standardized WHO in vivo procedure was used in CCCD activities to test for resistance to antimalarials. In this version, a younger group of children was examined to reflect the actual at risk group in most of sub-Saharan Africa. The test provides the clinical and parasitologic response information upon which policy can be based, and it also is suitable for frequent use in Malawi because it is feasible within the budgetary, personnel, and logistics constraints of the MOH. Because of the accuracy of results compared with in vitro test results and because of the immediate availability of results for use in policy formation, in vivo testing became an important means of monitoring resistance in Malawi and in other CCCD countries.

**Table CCCD Modification of WHO In Vivo Test**

	<b>WHO 7 day in vivo test (Bruce-Chwatt 1986)</b>	<b>CCCD modified test</b>
Ages of participants	6–14 years (usually)	<5 years
Parasite levels	≥800 asexual forms/mm <sup>3</sup> (usually)	>2000 asexual forms/mm <sup>3</sup>
Use of drugs	No history of antimalarial drugs for 1 week. Negative Dill-Glaxo urine test for 4-aminquinolines.	Negative Saker-Solomon test for 4-aminquinolines.
Blood smears	Thick and thin blood smears daily from Day 0 to Day 7, weekly to Day 28.	Thick and thin blood smears Day 0, Day 2, Day 3†, Day 7, Day 14‡, Day 28‡.
Health status of patients	Asymptomatic school children.	Preferentially symptomatic. Excluded if too ill to be treated orally. Axillary temperature taken each visit.
Follow up	Day 1 through Day 7, weekly to Day 28.	Day 2, Day 3†, Day 7, Day 14‡, Day 28‡.
Number of patients and analysis	At least 30 persons, but no definite scheme.	Dictated by statistical sampling using a modification of sequential analysis§.

† Day 3 follow up for those whose parasite densities on Day 2 had not decreased by 75%.

‡ Days 14 and 28 for assessment of hematologic response added in later studies.

§ Sample size was established to detect greater than 10% resistance or less than 1% resistance with 90% confidence. An initial group of 34 children was tested; the sample size was increased if the estimated prevalence of resistance fell between 1% and 10%.



**Study findings**

**II D 3 a (i) Efficacy of chloroquine**

***In vivo testing 1984-1986***

Because reports from another sub Saharan African country indicated that CQ in a single dose of 10 mg base/kg of body weight was effective one sentinel site tested this dosage among 26 children under 5 years 8 (30%) of the children showed an RIII response (see Box 4 for explanation of resistance patterns) and 21 (84%) of the remaining children showed an RII/RI response Therefore, testing at this dose was discontinued and continued with CQ in a dose of 25 mg base/kg body weight at this site and the five remaining sites

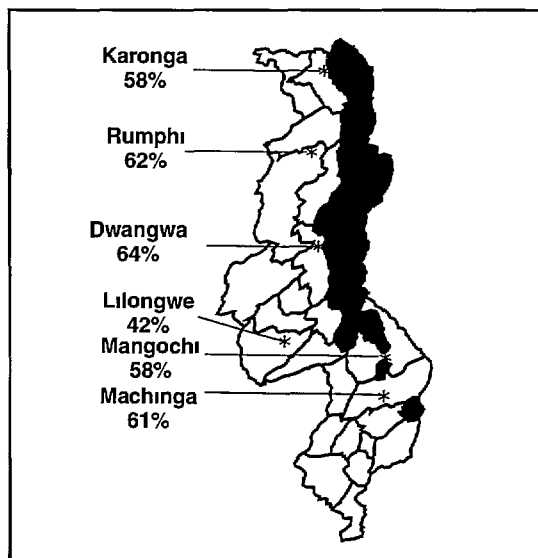
Results of testing children under 5 years of age and children between 5 and 10 years of age (Table 1) showed that CQ at the full curative dosage of 25 mg base/kg was not effective in eliminating parasitemia in a majority of children under 5 years of age, but that there was a trend towards greater CQ effectiveness among older children The studies suggested that an RIII pattern was present in 1984 among 8.5% of children less than 5 years old Although many individuals remained parasitemic on Day 7 the parasite densities among all but those with RIII patterns were markedly decreased by Day 7, and 92% of children under 5 who were febrile at the start were afebrile on Day 7 Older children had lower rates of resistant parasites no cases of RIII were observed

**Table 1 *P. falciparum* therapy failures to chloroquine 25 mg base/kg, in vivo testing, Malawi, 1984-1986**

Participant	Number	RIII pattern of resistance on Day 2 (%)	Failure to eliminate parasites by Day 7 (%)
Children < 5 years	246	8.5	57
Children 5-10 years	37	0	24

Resistance to CQ was shown to be widespread in the country as shown in Figure 13 of the results from the six sentinel surveillance sites

**Figure 13 Percentage of children less than 5 years of age with demonstrated chloroquine resistance (combined RI,RII,and RIII), by sentinel surveillance testing site, Malawi, 1984-1986**



#### II D 3 a (ii) Efficacy of second-line antimalarials

##### *In vivo testing 1984-1988*

In vivo testing at the sentinel sites was also conducted for second line antimalarials AQ (10 mg/kg and 25 mg/kg) and SP<sup>6</sup> (25 mg sulfa/kg) later mefloquine (MQ) (15 mg/kg) and halofantrine (24 mg/kg). Additional thick smears were collected on Day 14 and Day 21 for the two second line antimalarials AQ and SP (Heymann et al 1987) (Table 2). AQ and SP appeared fully effective however 34% of children receiving AQ were parasitemic 21 days after therapy. Resistance rates to AQ among children under 5 years appeared lower than to CQ.

<sup>6</sup>One tablet of SP is a fixed combination of 25 mg of pyrimethamine and 500 mg of sulfadoxine. SP is dosed at approximately 25 mg/kg of the sulfadoxine component.

**Table 2 Results of in vivo testing to second-line antimalarials, Malawi, 1985-1988**

Antimalarial (dosage)	Participants (children < 5 years)	Parasitemic children (%)		
		Day 7	Day 14	Day 21
Amodiaquine (10mg/kg) single dose	39	10	n t	n t
Amodiaquine (25 mg/kg) divided dose	37	3	18	34
Sulfadoxine pyrimethamine (25 mg sulfa/kg) single dose	34	0	0	0
Mefloquine (25 mg/kg) single dose	49	15	18	30
Halofantrine (24 mg/kg) divided dose	49	0	4	n t

\*n t = not tested

### II D 3 a (iii) Efficacy of quinine used for severe illness

Quinine was the standard treatment for severe and complicated malaria in Malawi baseline data to confirm 100% efficacy of quinine treatment was required for its continued use. Quinine in an 8 hourly dose of 10 mg/kg was tested at one of the sites among 25 children under 5 years of age who were admitted to the pediatric ward with *P falciparum* infections of >20 000 parasites/mm<sup>3</sup>. The children had 12-hourly thick smear examinations to determine parasite clearance time (i.e., the time when the first of two consecutive thick smears had no parasites). Parasite clearance times ranged from 36 to 108 hours with a mean of 67 hours, all children became parasite free.

### II D 3 a (iv) Clinical response to antimalarial drugs

#### **The question**

During the initial evaluation of CQ efficacy the study team observed that although parasite clearance was suboptimal, most individuals (children and adults) improved clinically following CQ therapy. While this led to continued use of CQ as the first-line antimalarial in Malawi, evaluation of the clinical response to antimalarials was carried out to further understand this issue.

#### **Study findings**

*Clinical response to CQ and SP* Twelve clinical signs and symptoms that had frequently been associated with *P falciparum* infection were examined for correlation with the density of parasitemias (Pappioanou et al 1991). Three of the clinical indicators were present in at least 75% of children with *P falciparum* infection and correlated with parasite density: history of fever during the preceding 48 hours, history of altered activity level during the preceding 48 hours, and axillary temperature >37.2°C. These three indicators were used to compare children's clinical response to CQ and to SP. By Day 2, CQ was shown to have a more rapid effect in alleviating symptoms consistent with its more rapid schizonticidal activity and its antipyretic effect. By Days 7 and 14, however, clinical failure rates for CQ were not significantly higher than for SP, though considerable numbers of children in both groups remained ill (Table 3).

**Table 3 Clinical response to chloroquine and sulfadoxine-pyrimethamine, measured by three clinical indicators, Malawi**

Antimalarial (dose)	Participants (children <5 years)	≥1 of 3 clinical indicators present			
		Day 0 (%)	Day 2 (%)	Day 7 (%)	Day 14 (%)
Chloroquine (25 mg base/kg)	126*	95	48	29	32
Sulfadoxine pyrimethamine (25 mg sulfa/kg)	40	100	78	10	15

Three of the 126 children were excluded from the study between Days 2 and 7 because of persistent high fever and treated with amodiaquine 15 of the remaining 123 were excluded from further analysis and treated between Days 7 and 14

*Clinical response to quinine* Axillary temperature was selected to monitor the time to fever clearance during in vivo testing of quinine (see study described above) Fever clearance time was defined as the time when the axillary temperature first fell below 37.5° C and remained below this level for 48 hours The mean fever clearance time after treatment with quinine was 36 hours (the range was between 12 and 72 hours) the mean parasite clearance time was 67 hours

### **Impact on policy**

On the basis of the findings from these in vivo studies a malaria therapy policy was established in 1985 that endorsed the 1983 decision to discontinue routine chemoprophylaxis for children less than 5 years old and recommended immediate presumptive treatment of fevers using CQ in a dose of 25mg base/kg Although parasite resistance to CQ had been demonstrated CQ remained the drug of choice because of its efficacy in reducing clinical illness in the 7 days after therapy its wide availability and general safety A dose-for age chart showing correct CQ doses for age was developed for use in all health facilities and by other health care providers (village health workers and TBAs)

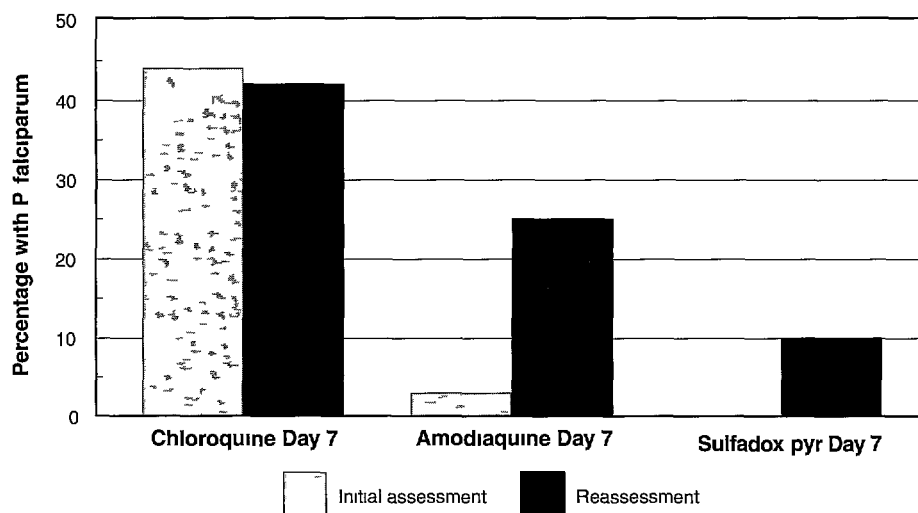
Because of their superior effectiveness among children under 5 years who had high levels of CQ resistant *P falciparum* AQ and SP were recommended as therapy for CQ treatment failures It was further recommended that suspected chloroquine resistant infections be evaluated by thick smear before beginning alternative treatment although this was possible only at the larger health facilities

## **II D 3 a (v) Reevaluation of in vivo response to antimalarials**

### **Study findings**

Initial CQ AQ and SP resistance testing was completed in 1984 and 1985 In 1986 and 1987 in vivo response to CQ (25 mg base/kg), and SP (25 mg sulfa/kg) was reassessed to monitor changes in *P falciparum* response to these drugs (Figure 14) AQ had a significantly poorer Day 7 response compared with SP suggesting that resistance to antimalarials in Malawi was continuing to intensify

**Figure 14** Changing in vivo response to antimalarials initial testing vs reassessment, Malawi, 1984-1987



### **Impact on policy**

The changes in parasite response measured by repeat in vivo testing were not considered sufficient to warrant a change in the treatment policy in view of concurrent studies of clinical response to antimalarials. However, because continued evolution of drug resistance was anticipated in Malawi, a policy of routine reassessment of *P. falciparum* response at the sentinel sites was recommended, with immediate in vivo testing if unsolicited reports of change in clinical response to treatment were received from anywhere in the country.

## **II D 3 b Prevention of perinatal malaria**

### **Study findings**

**Efficacy of prophylaxis with CQ** CQ efficacy was examined among pregnant women who were given weekly prophylaxis under observation in a dose of 300 mg base (the National Policy) to determine the effectiveness of CQ in keeping peripheral blood and placentas free of *P. falciparum* parasites (McDermott et al 1988). Seventy-three women who had either no initial *P. falciparum* parasitemia or initial parasitemia that had cleared after treatment with CQ or AQ (25 mg/kg) were followed from early in the second trimester of pregnancy until delivery, with thick smears every 2 weeks. Among these 73 women, 25% had *P. falciparum* parasites detected at some time during prophylaxis. The geometric mean parasite density of breakthrough infections was 145 parasites/mm<sup>3</sup>; parasite patency was asymptomatic among 89% of the parasitemic women, and the majority of women who had parasite breakthroughs were observed to clear parasitemias spontaneously during continued prophylaxis. Thirty-six women in the group delivered in hospital and had placental specimens collected. These women were much less likely to have had evidence of active or past infection compared with women delivering at the same hospital but not enrolled in the study (56% vs 92%, respectively) ( $p=0.0005$ , chi-square).

**Efficacy of antimalarial treatment in pregnant women** In 1987, antimalarial treatment with CQ, AQ, and SP was examined in pregnant women using a standard in vivo drug sensitivity study methodology (Table 4). CQ was the least effective, with 21% of women having persistent parasitemia on Day 7.

**Table 4** In vivo test results of *P. falciparum* resistance to chloroquine, amodiaquine, and sulfadoxine-pyrimethamine in pregnant women, Malawi, 1987

Drug tested (dosage)	Number of women	Initial GMPD*	Parasitemic on Day 7 N (%)	Parasitemic on Day 14 N (%)	Parasitemic on Day 21 N (%)	Parasitemic on Day 28 N (%)
Chloroquine (25 mg base/kg)	33	3188	7 (21)	8/31* (25)	9/31 (29)	12/28 (43)
Amodiaquine (25 mg/kg)	24	2239	1 (4)	1/22 (5)	3/22 (14)	9/15 (60)
Sulfadoxine pyrimethamine (25 mg sulfa/kg)	38	3677	0	0	0/31	0/24

GMPD = geometric mean parasite density

\*\* The number of women followed for  $\geq 14$  days varied due to delivery or loss to follow up

In 1988 in vivo studies with 21 day follow up of MQ efficacy in pregnant women showed results similar to those seen in studies of the highly efficacious SP

#### **Impact on policy**

The results of evaluation of both treatment and prophylactic doses of antimalarials demonstrated that CQ was not optimally effective for either type of drug use in pregnant women in Malawi. This led to the development of the MMRP to examine malaria prevention efforts in pregnancy (see Box 6). These results also established a knowledge base among MOH staff and an environment that would be responsive to new information regarding an effective intervention during pregnancy — setting the stage for new policy decisions with the completion of the MMRP and further evaluation of other drugs.

### **Box 6 The Mangochi Malaria Research Project (MMRP)**

In a longitudinal study conducted from September 1987 through June 1990 4 220 pregnant women were enrolled in four antenatal clinics in Mangochi District and assigned one of four regimens of antimalarial treatment and/or chemoprophylaxis

- 1 Chloroquine (CQ) treatment dose of 25 mg base/kg as a divided dose over 2 days followed by 300 mg weekly
- 2 CQ treatment dose of 25 mg base/kg as a divided dose over 2 days and repeated every 4 weeks
- 3 CQ 300 mg base weekly (Malawi National Policy)
- 4 Mefloquine (MQ) treatment dose of 750 mg as a single dose followed by 250 mg weekly

Each dose of medication was given under observation by a study team member either at the clinic or at home the women were followed at 4-week intervals until delivery after which mothers and infants were seen approximately every 2 months

**At-risk groups** The study confirmed earlier findings that pregnancy number was an important determinant of malaria infection in the women her placenta and the umbilical cord blood of the newborn with primigravidas carrying the highest risk The study also found the incidence of low birth weight (LBW) by parity group to be higher for babies born to women with placental malaria infection than for those without placental malaria The association between placental malaria infection and LBW in firstborns was strongest among women whose third trimester of pregnancy was exposed to high malaria transmission during the rainy and early post-rainy season

**Efficacy of antimalarials in clearing placental infection** Mefloquine was much more likely than CQ to clear placental infection Of the primigravidas assigned to one of the CQ regimens 46% had placental malaria infection compared with 9% of the primigravidas receiving MQ Mefloquine was more effective among multigravidas as well 15% receiving CQ and 3% receiving MQ had placental malaria infection In each parity group the incidence of LBW was lower for women who had no placental malaria, regardless of the drug used to keep the placenta parasite free

**Efficacy of antimalarials in clearing peripheral infection** Parasitemia at delivery was 23.4% in primigravidas 15.7% in secundigravidas and 10.1% in multigravidas The peripheral parasitemia rate in women given CQ was more than five times that of women given MQ, confirming the markedly different efficacy of the two drugs

**Umbilical cord blood infection** Umbilical cord blood malaria infection was identified in 6.7% of newborns and was correlated with the density of placental malaria infection umbilical cord blood malaria was associated with preterm LBW

**LBW and survival** LBW was found to be a major determinant of neonatal and infant survival Compared with babies of normal birth weight babies born in the lower weight groups of 2 000–2 499 grams 1 500–1 999 grams and below 1 500 grams were 2.4, 11.5, and 27.1 times more likely to die in the neonatal period Infants born with LBW had a 1.4 fold higher risk of dying in the postneonatal period than their counterparts of normal birth weight In this study malaria infection in pregnancy was found to account for as much as 12% of LBW babies

#### **Impact of the MMRP on policy**

The MMRP showed that a program of chemoprophylaxis for pregnant women with an efficacious drug could be successful in reducing a significant amount of LBW After discussions of the results of the MMRP at the 1991 national meeting in Mangochi the National Malaria Control Committee decided that CQ should be replaced by a more effective drug for malaria prevention during pregnancy Although MQ had been found effective it was not feasible for national use due to its cost and lack of availability The committee initiated studies to select an alternative antimalarial for a national program of malaria prevention (Section II D 2)

### II D 3 c Treatment of severe malaria

#### ***The questions***

Although guidelines for the management of cerebral malaria had been established in the 1985 National Malaria Plan important unresolved issues in the understanding of cerebral malaria and its treatment remained. First the lack of a uniform simple and practical method to assess the severity of impairment of consciousness among children with cerebral malaria hindered comparison of the efficacy of different antimalarial regimens. Second prognostic factors for adverse outcomes in children with cerebral malaria were poorly understood. Third it was unclear to what extent the decreased plasma glucose frequently observed in cerebral malaria was related to malaria disease or to quinine induced hypoglycemia (Box 7). Finally further information was needed concerning the proper dosage and administration of parenteral quinine in children with cerebral malaria. These issues were addressed through research conducted in the Malaria Research Project at the Department of Pediatrics at Queen Elizabeth Central Hospital (QECH) in Blantyre from 1986 to 1988.

#### ***Study findings***

*Uniform measurement of illness severity* To provide a uniform method of measuring the level of obtundation in children with cerebral malaria a grading system was developed based on modifications of the Glasgow scale used for unconscious adults (Teasdale and Bennett 1974). This modification uses motor and crying responses to pain as well as the ability to watch or follow objects to grade the severity of depression of consciousness in very young preverbal children (Molyneux 1989b). The Blantyre coma scoring system has been widely adopted by cerebral malaria researchers throughout the world (WHO 1990).

*Risk factors for adverse outcomes* Among children admitted to QECH with cerebral malaria clinical signs (e.g. profound coma, convulsions at the time of admission) as well as laboratory indicators (e.g. hypoglycemia, hyperparasitemia) were associated with a poor outcome. Fifteen percent of children died and 9% were left with neurologic sequelae. A prognostic index based on some of these risk factors more accurately predicted outcome than any single feature. These data helped to elucidate the natural history and prognosis of cerebral malaria. Use of the Blantyre coma scale enabled researchers to compare the severity of cerebral malaria among groups of children to evaluate various therapies.

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#### **Box 7 Hypoglycemia and cerebral malaria**

Hypoglycemia is common in children with severe falciparum malaria and is associated with increased mortality (White et al 1987). Preliminary data had suggested that intravenous quinine infusions caused excessive insulin secretion and hypoglycemia (Okitolonda et al 1987). The importance of hypoglycemia and the question of whether quinine induced hyperinsulinemia occurs was evaluated in children with cerebral malaria at QECH (Taylor et al 1988b).

Among patients with pretreatment hypoglycemia 37% died and 26% had neurologic sequelae. In contrast among normoglycemic children only 4% died and 7% had residual sequelae. The worst prognosis was associated with recurrent hypoglycemia. No children who were normoglycemic on admission became hypoglycemic during treatment with intravenous quinine. Hypoglycemia during quinine treatment occurred only among children who were hypoglycemic on admission and it was not associated with hyperinsulinemia.

Information from these studies documented that hypoglycemia was a common and serious complication of cerebral malaria in Malawian children and provided reassurance that slow intravenous quinine infusion to children on maintenance therapy with glucose did not contribute to the risk of subsequent hypoglycemia.



*Quinine route of administration and dosage* Although intravenous quinine is recommended for treatment of severe malaria children with cerebral malaria may initially present at peripheral health centers where intravenous therapy may not be available. In such situations, administration of intramuscular quinine might be a practical alternative, however, the efficacy, safety, and pharmacokinetics of intramuscular quinine in children with severe malaria were largely unknown. In a study of children with severe malaria at QECH, patients treated with intramuscular quinine (initial dose 10 mg/kg body weight) cleared their parasitemia and had no significant adverse clinical effects (Mansor et al 1990).

Because cerebral malaria can be rapidly fatal it is important to achieve effective plasma quinine concentrations quickly and safely. Questions remained about how quickly effective quinine blood concentrations were achieved with the 1985 National Malaria Plan regimen of 10 mg/kg body weight every 8 hours. Previous research had suggested a loading dose of quinine (20 mg/kg body weight intravenously over 3 hours) might be beneficial, but there were concerns about the potential toxicity of such a regimen in severely ill children (White et al 1983). Pharmacokinetic and clinical studies conducted at QECH showed that loading dose therapy resulted in rapid achievement of effective plasma quinine concentrations and was not associated with undue risk of toxicity (Taylor et al 1988b). A more rapid rate of quinine infusion (1 hour) was associated with relatively increased plasma insulin levels and a potentially increased risk of hypoglycemia compared with the standard infusion rate (Molyneux et al 1989c).

### ***Impact on policy***

During 1988 and 1989, the data from the QECH Malaria Research Project were presented and discussed in meetings with MOH and other medical personnel throughout Malawi, and at the national meeting in Mangochi in 1991. As a result of these discussions, the national malaria guidelines were revised. The recommended management of severe malaria was modified to reflect the newly available information in the following ways:

- 1) Patients with severe malaria diagnosed in the outpatient setting should be treated with intramuscular quinine in a dose of 10 mg per kg body weight to be repeated at 4 hours and every 12 hours thereafter until transport to a facility where intravenous therapy is available.
- 2) Hypoglycemia should be actively evaluated and corrected,
- 3) In inpatient settings, quinine therapy should be initiated with a loading dose of 20 mg/kg body weight given intravenously over 3 hours,
- 4) During therapy, the degree of impaired consciousness should be monitored with the Blantyre coma scale assessment, and
- 5) After recovery, the child should be assessed 2-4 weeks post hospitalization for neurological deficits and, if appropriate, physiotherapy should be initiated.

## **II D 4 Studies of malaria treatment and prevention practices**

### **II D 4 a Malaria treatment and prevention practices in the community**

#### ***The questions***

To help design methods of providing CQ at the community level through the PHC system current treatment practices in the community were studied. Several small scale PHC projects, sponsored by the ACSI CCCD Project and other organizations, were established. Evaluations were conducted to determine the proportion of those with malaria treated at home (versus health facility), correct treatment with CQ at home and the acceptability of TBA-based treatment in communities.

### **Study findings**

*Home treatment* Two surveys and a special sentinel surveillance system<sup>7</sup> provided information about community practices nationally and in Salima District along the lakeshore. Estimates from two surveys of the proportion of children who were treated at home for malaria ranged from 31% to 54%. The surveys and surveillance system showed that CQ and antipyretics had been given to only a minority of febrile children. Eight to fifteen percent of children under the age of 5 years who had fever/malaria within the previous 2-week period had been treated at home with CQ, and 1%–18% had been treated with an antipyretic.

*Acceptability of TBAs as community health providers of CQ* A study conducted in 47 villages in Salima District showed that TBAs could safely provide CQ treatment in the community. TBAs in one third of the villages (study villages) were trained in the presumptive diagnosis and treatment of fever/malaria and given a supply of CQ. Meanwhile, health staff in all health facilities serving the villages were given refresher training in the diagnosis and treatment of malaria. Study village chiefs advised community members that they could receive free treatment in the community from a TBA. After 6 months, 56% of the women in the study villages and 5% of the women in the control villages consulted a TBA for malaria treatment for their children. TBAs provided correct doses of CQ to 92% of the children they saw, while correct doses were recorded for only 18% of the children treated by health workers ( $p < 0.0001$ ). However, to use TBAs to deliver CQ in the community required more funds for their training and supervision.

### **Impact on policy**

Although the GOM 10 year health plan recommended that an increasing proportion of all health services be conducted in the community by mothers and community health workers (e.g., village health workers, TBAs), the overriding concern of the Malaria Control Program was that fever should be treated promptly with an antimalarial. While the above data do not reflect timing of treatment, they do show that 50%–70% of all febrile children were treated at a health facility. Nationwide at the community level, few caretakers were using CQ and antipyretics in the home. This finding could reflect either lack of physical or financial access to CQ in the community or lack of knowledge of appropriate treatment of febrile illness. Attempts to improve CQ use in the community by equipping TBAs to be providers, although successful in the study in Salima District, were costly and could not be sustained.

## **II D 4 b Outpatient and inpatient treatment practices**

### **The questions**

To evaluate the extent to which health workers were complying with the new national malaria treatment guidelines of 1985 and to provide baseline data for monitoring health worker training, outpatient and inpatient treatment practices were examined.

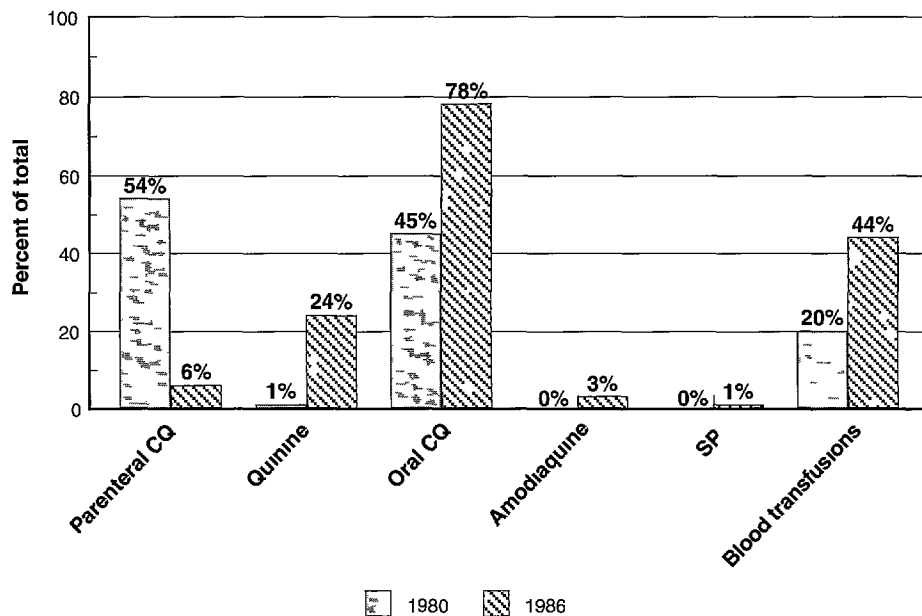
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<sup>7</sup> Home treatment practices of parents and guardians whose child with a fever or malaria was being seen at a health facility were monitored through a special sentinel surveillance system established in 1986 at 12 outpatient facilities representative of the geographic and climatic areas of the country. A surveillance officer from each site, selected from among the hospital clinical staff, was trained in interview technique, sentinel reporting, and basic data analysis during a 1 week training course. Each sentinel facility was provided with a preprinted register for recording daily surveillance information about all children under the age of 5 years presenting with fever/malaria. Data on what treatment, if any, was provided before the child arrived at the health facility, what treatment was given at the health facility, and whether the child was referred for admission to an inpatient facility were recorded.

**Study findings**

*Antimalarial drugs and transfusions administered as inpatient treatment* At one of the sentinel sites, records were reviewed for all children who were admitted during the years 1980 through 1986 with malaria as one of their discharge diagnoses. Treatment patterns in hospital reflected correctly implemented policy recommendations during the years 1984 to 1986 and were consistent with increasing use of oral antimalarial drugs other than CQ and use of oral CQ (in contrast to parenteral CQ) (Figure 15). The 50% increase in blood transfusions was consistent with increasing numbers of children being admitted with anemia.

**Figure 15** Recorded use of antimalarials and blood transfusion among hospitalized children with malaria, Malawi, 1980 and 1986



N=8454 children with malaria as a discharge diagnosis

*Health worker practices in an outpatient facility* In one study 86 health workers were trained in a refresher course in methods of diagnosis and presumptive treatment techniques and then evaluated 12 months later. Although 90% of the health workers prescribed CQ for the children and 52% measured the child's temperature, fewer than half asked the age of the child or gave the first dose of CQ in the health facility, and fewer than one in four prescribed the correct dose of CQ for age or gave an antipyretic.

**Impact on policy**

*Inpatient practices* The Malaria Control Program recommended that monitoring of treatment practices be continued at this and other sentinel site hospitals. Because of this record review, the program recommended limiting the use of blood transfusion in children with malaria whenever possible until safe blood supplies (i.e. blood screened for human immunodeficiency virus) could be ensured at all hospitals.

*Outpatient practices* Although refresher training of health workers appeared to result in health workers administering presumptive doses of CQ, workers did not give the correct dose or give an antipyretic as an adjunct to treatment. A recommendation was made to modify refresher training to include practical experience. However, this recommendation was not implemented.

#### **II D 4 c Antimalarial use among pregnant women**

##### ***The questions***

The effectiveness of antimalarial prevention during pregnancy relies on both the efficacy of the drug (see above Section II D 2 b ) and the woman s compliance with the recommended regimen Increased understanding of compliance and determinants of compliance among pregnant women was sought

##### ***Study findings***

*Compliance to antimalarial prophylaxis among pregnant women* Although sufficient quantities of CQ tablets of 150 mg base were provided to pregnant women attending ANCs to take the recommended dosage at home (two per week between monthly clinic visits), compliance rates were not high Eight hundred and two women attending ANC at four of the sentinel sites 160 of whom were on first visit, were asked to provide a urine specimen to determine levels of CQ and desethyl chloroquine (Heymann et al 1990) Of those women on first visit 20% had urine CQ levels compatible with ingestion of a CQ prophylactic dose (5 mg base/kg) during the preceding 7 days and 36% of those on return visit had compatible CQ levels ( $p=0.0002$  chi-square) In addition to urine testing thick smears were collected from pregnant women at these same clinics and examined for *P falciparum* parasites Among 280 women on their first ANC visit 40% had *P falciparum* parasites identified on thick smear while among the 728 women on return visit 31% had *P falciparum* infection

Intervention efforts to improve compliance with CQ prophylaxis were conducted in four clinics in Lilongwe District The three interventions used (improved health education use of a sugar-coated CQ tablet to eliminate the bitter taste or both) were found to be associated with significant increases in improved compliance with CQ ingestion (Helitzer Allen 1993a)

##### ***Impact on policy***

These results suggested that poor compliance with home ingestion of antimalarials was a major impediment to the effectiveness of the program In fact the overall effectiveness of antenatal CQ prophylaxis programs in Malawi was determined to be less than 10% of the maximum theoretical effectiveness, which is based on the use of a 100% efficacious drug and 100% compliance These results suggested to MOH officials that any regimen that used an antimalarial more efficacious than CQ and that reduced the effect of poor compliance (e.g. simpler dosing regimens or in clinic dosing only) would be much preferred over the existing regimens which required home ingestion of CQ

## II E Impact on studies on policy a summary

From 1984 through 1989, data collected and evaluated from routine monitoring systems (the national HIS), special surveillance systems (e.g., malaria sentinel surveillance), and a series of field studies provided both baseline information on the malaria situation in Malawi and important information on which to base policy and program strategies. This information was summarized by topic in the previous section, and some of the chief points are highlighted below.

*The problem of malaria* The documentation of high malaria-related morbidity and mortality in the early prevalence studies and through the HIS provided support for the intense control efforts expended by the GOM and the international community. Studies of the problem of malaria were able to provide justification for the target groups—children under 5 years of age and women in their first and second pregnancies. Studies showing the latter group at greater risk than women in later pregnancies led to changes at the national level in the priority given to malaria treatment and prevention among pregnant women. Prevalence surveys revealing increasing rates of anemia in hospitalized young children constituted an additional argument for the need for continued reassessment of the efficacy of the first-line antimalarial.

*Malaria interventions* Clinical and parasitologic responses to CQ obtained from *in vivo* studies throughout the country provided essential information for policy formulation and revision and the development of standard treatment guidelines. On the basis of findings from these studies, the 1985 policy recommended halting routine chemoprophylaxis for children less than 5 years old and treating fever presumptively with CQ in a dose of 25 mg base/kg. Although CQ was decreasingly effective in clearing parasites, 1984–1986 data on clinical response indicated that it retained its effectiveness in reducing symptoms. Because it was clear that CQ resistance was increasing, a policy of routine reassessment of response was recommended. Studies showing that CQ was not optimally effective for pregnant women in either a treatment or prophylactic dose led to the examination of more effective antimalarials, SP and MQ. Although MQ was used as a highly effective antimalarial drug for pregnant women in a large study in Malawi (MMRP), it was understood that it could not be recommended for national policy because of its expense and lack of availability, and the committee initiated additional studies to examine a potentially effective, safe, and affordable alternative antimalarial.

*Malaria practices* Studies found that children were not being treated correctly at home or at health facilities. The malaria control program then attempted to improve community CQ use by equipping TBAs as providers, a strategy that, while effective, was too costly to be sustained. The program also recommended ongoing monitoring of malaria treatment at health facilities and providing refresher training to workers. Pregnant women's compliance with a regimen of antimalarial prophylaxis was poor, chiefly because the drugs had to be taken at home. These data laid the foundation for MOH commitment to find a more effective regimen that would reduce noncompliance as an impediment to program effectiveness.

Early operational research yielded these lessons:

- A systematic approach toward policy, strategy, and guideline development was critical for the orderly development and success of a national policy, plan, and program. These steps included a) engaging decision makers early in the process, b) gathering important information on the problem of malaria, the efficacy of interventions, and existing patient and health worker practices, c) establishing a formal national program with an oversight/advisory committee with clear organization and responsibilities, d) elaborating a national policy and plan, e) developing and disseminating treatment and prevention guidelines, f) preparing health education and training.

materials, and g) convening broad-based meetings for consensus building on policy and program planning and information dissemination

- Documentation of the problem was important it provided an opportunity for the national program staff to develop experience in basic malaria issues, and it showed senior officials and donors the extent of the problem and its relative importance in Malawi. The information also provided a baseline against which progress could be measured. However, documentation of the problem alone was not sufficient to engender support for malaria control efforts. Evidence of success with interventions was lacking, and the Ministry and donor community had not strongly committed resources (personnel or money) to address the problem.
- Because the National Malaria Control Policy adopted strategies based principally on the therapeutic and preventive use of antimalarials, it remained important that the efficacy of these interventions be monitored.
- It is in the area of practices (health worker, patient, and caretaker) that the majority of shortcomings in program effectiveness were documented. At the same time, while improvements in these areas were recommended, their implementation was limited by shortfalls in resources — particularly for training, refresher training, and supervision.

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## CHAPTER III

# Evaluating and Refining the Malaria Control Policy and Program: 1989-1993

'Part III Evaluating and refining the malaria policy and program 1989-1993 describes the external evaluation of the first 5 years of the malaria control program and the subsequent history of Malawi's process of policy and program development. As in Part II, the studies reviewed are categorized by focus problem, interventions, and practices.

### III A Summary of malaria program and policy accomplishments

In 1989, Malawi's malaria control program was evaluated by a group composed of Malawians from the MOH and nongovernmental organizations and external consultants from international organizations. The shortcomings identified, chiefly in the area of program implementation, led to a revised control plan for 1990-1994. In addition, on the basis of studies of antimalarial efficacy in children under 5 and pregnant women, the program officially changed its first-line drug from CQ to SP.

**Figure 16 Malaria program and policy milestones 1990-1993**

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1990	1991	1992	1993
Developed malaria control plan	Approved malaria control plan Revised treatment guidelines at national meeting in Mangochi	Updated and printed treatment guidelines Held meeting with private sector pharmaceutical companies Conducted health education materials development workshop Held regional meetings (92 '93) to announce antimalarial change	Implemented change in first line antimalarial drug Established system to track effects of SP Trained sentinel surveillance personnel

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**Figure 17 Studies affecting malaria policy development 1990-1993 \***

1990	1991	1992	1993
Parameters to evaluate antimalarial efficacy			
Clinical diagnosis and treatment of overlap malaria and pneumonia			
	Assessment of malaria vectors		
		Regimen for preventing malaria in pregnancy	
		Knowledge attitudes, and practices malaria in children & pregnant women	
		Economic cost of malaria	
		Evaluation of presumptive treatment and case definition of malaria	

Time line shows the year in which the studies were begun

### III B The 1989 evaluation of the first five years

In July and August 1989, an evaluation of the malaria control program was conducted. Six external consultants from UNICEF, USAID and WHO, and 22 Malawians drawn from the MOH and nongovernmental organizations participated in the evaluation. The purposes of the evaluation were to determine whether the objectives for the first 5-year plan (1985-1989) had been achieved and to identify problems in achieving the objectives that could be addressed in the subsequent 5 years. The evaluation consisted of interviews with officials at the MOH, hospitals and other health facilities, assessment of health worker job performance, health facility record review, and a KAP survey. For the KAP survey, 30 clusters throughout the country were randomly selected using the Expanded Programme on Immunization cluster sample survey methodology, and information was collected using questionnaires and other forms developed for the evaluation. Specific objectives were to 1) assess malaria control activities in Malawi and determine the degree of success in achieving established goals, 2) identify technical and operational problems, 3) determine solutions for accelerating implementation of malaria control strategies, and 4) develop guidelines for the 1990-1994 implementation plan.

A 2-day training session was conducted to familiarize team members with procedures and evaluation materials. Following the training, the review team was divided into five groups, each with at least one external consultant as team leader. The groups visited the three main referral hospitals, 16 district hospitals, 30 health centers, and 870 households.

*Assessment of success in reaching goals* Health facility data showed that the objectives to reduce malaria morbidity and mortality in Malawi had not been achieved. From 1985 to 1988, under 5 hospitalization increased by 43%, hospital deaths grew by 85%, and malaria case fatality rates rose by 30%. While the worsening of chloroquine-resistant malaria was thought to be the major cause for failure to achieve program objectives, programmatic and operational problems were believed to have contributed to limiting program success.

*Programmatic and operational problems identified* The malaria control program suffered from four main management constraints:

- Operational plans did not exist at all levels. The 1985-1989 implementation plan was seen largely as a strategy/policy document because it lacked a timeline for program implementation. The regional and district personnel lacked a clear vision for planning, considering it chiefly in terms of training activities.



- Management personnel responsible for planning, implementing, monitoring, and supervising malaria control activities at the national, regional, and district levels were insufficient in number, sometimes inadequately trained, and burdened with other responsibilities
- There was no budget for malaria control. No record existed to show how much had been spent, how much was needed, or how much was available for malaria control at any of the three levels
- Supervisory activities at all levels were sporadic, not carefully planned, and unguided by specific performance, standard, or target criteria

*Ineffective training* Between 1985 and 1989, numerous malaria training activities were carried out, mostly for senior and midlevel managers from the national, regional, and district levels. However, it was not possible to determine the effectiveness of these training activities since there were no reports of these activities at each level of health delivery. Some of the personnel carrying out malaria activities had no formal training, most lacked the experience and skills necessary to train others, and thus the content of training activities was not always adequately transmitted. The sessions were often too short, highly didactic, with little opportunity for practical work, and not followed by review, refresher courses, or supervisory visits. Documentation of training and other program components was largely inadequate.

*Inadequate health education* Malaria health education materials were developed by the Health Education Unit of the MOH, with assistance from the Healthcom Project, starting in 1986. More than a dozen innovative items designed to educate mothers and health workers were widely distributed in all districts, and regional and district personnel participated in 3-day workshops on their use. Despite this base of achievement, health education for the malaria control program experienced serious shortcomings.

- The use of the health education materials was poorly understood within the Health Education Unit, consequently, training in their use was inadequate. In addition, many health center personnel responsible for teaching mothers and pregnant women about malaria management and prevention did not receive any training in the use of these materials and in health education methods in general.
- Behavioral research to support the development of the materials was inadequate in scope of enquiry and regional coverage. These weaknesses were thought to contribute to underutilization of the materials.

*Outcome of evaluation* The 1990-1994 malaria control plan was based on results of the evaluation and was designed to address the identified constraints. This plan provided more details of program implementation and included a time line for major program activities. A more extensive, nationwide KAP survey (discussed in II D 3) was conducted to better understand the community's awareness of malaria and to develop appropriate health education materials.

In 1991 and 1992, to address the severe shortage of technical assistance, two external experts were hired to provide technical support for the malaria control program. During the same period, two nationals were sent abroad for advanced training. The program appointed an additional health worker whose sole responsibility was malaria control management.

### **III C Refining the malaria control policy and program 1990-1993**

Guided by the 1989 evaluation, the second 5-year malaria control plan (1990-1994) was developed in 1990 and approved in 1991. To reach its targets, the reduction of malaria-related mortality and morbidity by 10 percent and 20 percent, respectively, the plan identified ten necessary elements

- Improved understanding of malaria illness, prevention, and treatment
- Accurate diagnosis
- Effective treatment
- Effective prevention in high-risk groups
- Alternative control methods
- Diagnosis, treatment, and reporting incorporated into health personnel training
- Strengthened malaria reporting system
- Effective management and administration of the Malaria Control Program at all levels
- Increased research capability
- Increased GOM and donor investment in malaria control

For program activities, a time line was drawn up and the responsible office and support agency were noted where applicable. Information was gathered, and actions were taken for each of these items (Table 5), which are discussed further in Section III D

**Table 5 Studies and activities conducted to address the ten elements of the 1990-1994 national malaria control plan**

<b>Element of National Malaria Control Plan</b>	<b>Studies and Activities during 1990-1993</b>
Improved understanding	Knowledge, attitudes, and practices (KAP) survey to document existing understanding and practices health education material development based on KAP findings
Accurate diagnosis	Studies to examine diagnostic criteria and improve clinical diagnosis of malaria
Effective treatment	Studies to examine clinical and hematologic outcomes as measures of effective treatment, change from chloroquine (CQ) to sulfadoxine pyrimethamine (SP) as primary therapy for malaria*
Effective prevention in high risk groups	Studies to examine feasible regimens for malaria prevention in pregnant women led to change in national policy for malaria prevention in pregnancy
Alternative control methods	Assessment of malaria vectors biting habits entomologic inoculation rates planning for work with insecticide impregnated bednets
Incorporation of diagnosis treatment and reporting into health personnel training	**
Strengthened malaria reporting system	**
Effective management of malaria control program all levels	National level increased staff training for a Malawian at epidemiologist with malaria experience Regional level designated responsible person for malaria control supervision
Increased research capability	Doctoral and master's level training for two Ministry of Health (MOH) staff with emphasis on training in malaria control issues
Increased Government of Malawi (GOM) and donor investment in malaria control	Economic assessment helped the GOM and donors understand current expenditures MOH provided financial commitment to change from CQ to SP donor interest increased but investment amount not greatly changed

\*Highlighted in Box 9

\*\*As of the end of 1993 no activities had addressed this element

### **III D Information gathered and its effect on malaria policy**

#### **III D 1 Operational research agenda 1990-1993**

Because the program evaluation showed rapidly increasing malaria-related morbidity and mortality and weaknesses in program delivery, the malaria control committee sponsored additional studies to refine the malaria control policy and refocus the malaria control program.

*The problem of malaria* The difficulty in diagnosing malaria definitively on the basis of clinical features (laboratory confirmation being generally not possible due to lack of microscopy) and the frequently overlapping diagnosis of malaria and pneumonia, another frequent childhood illness, led to studies examining the overlap of these two illnesses. To further understand the role of alternative measures for malaria control, an assessment of local malaria vectors was conducted, both to train a cadre capable of monitoring vectors and to evaluate the feasibility of insecticide-impregnated bed nets as a locally relevant control measure. In addition, the committee recognized that to allocate scarce resources most wisely for effective interventions, the economic cost of malaria to families and to the nation must be assessed.

*Malaria interventions* The continuing efficacy of CQ was questioned because anemia was becoming an increasing cause of hospital deaths among children. Studies had shown that CQ was increasingly ineffective in clearing parasitemia, and persistent and/or recurrent parasitemia was known to result in anemia. Studies were then conducted to assess the current efficacy of CQ parasitologically, clinically, and hematologically and to determine whether an alternative drug (SP) would be more efficacious. Earlier studies of the use of CQ in regimens of treatment and prophylaxis among pregnant women had conclusively shown that CQ no longer retained sufficient efficacy, during this period, the committee focused on finding an antimalarial that could be used in a nationwide program of malaria prevention in pregnant women.

*Malaria practices* To launch the new first-line antimalarial, practices of people in the community had to be explored—their beliefs about the disease and its treatment and their own actions to prevent and cure malaria. With this information, effective health education messages could be designed, and subsequent policy changes could be monitored and evaluated.

The next sections review the results of studies conducted to evaluate the problem, interventions, and practices. The question(s) to be answered by the study and the study findings are followed by a summary of the effect of each study on Malawi's malaria policy.

#### **III D 2 Studies of the problem of malaria**

##### **III D 2 a Case definition of malaria**

###### ***The questions***

In Malawi and in most of sub-Saharan Africa, the national policy for malaria treatment is to presume that a person with fever or recent history of fever has malaria and to provide treatment with an antimalarial drug. This presumptive treatment strategy, developed in the late 1970s and early 1980s, was based on clinical rather than laboratory findings because microscopic confirmation of malaria parasitemia was rarely possible and even where possible prohibitively expensive. At the same time that effective therapy was being reconsidered (see IV D 2), the MOH began to reconsider the presumptive treatment strategy. Three studies were undertaken to examine 1) the overlap

between the clinical diagnosis of malaria and acute respiratory infection (ARI) in children, 2) alternative clinical case definitions for malaria in children, and 3) presumptive versus laboratory diagnosis of malaria in adults

**III D 2 a (i) Clinical diagnosis of malaria and ARI**

**The question**

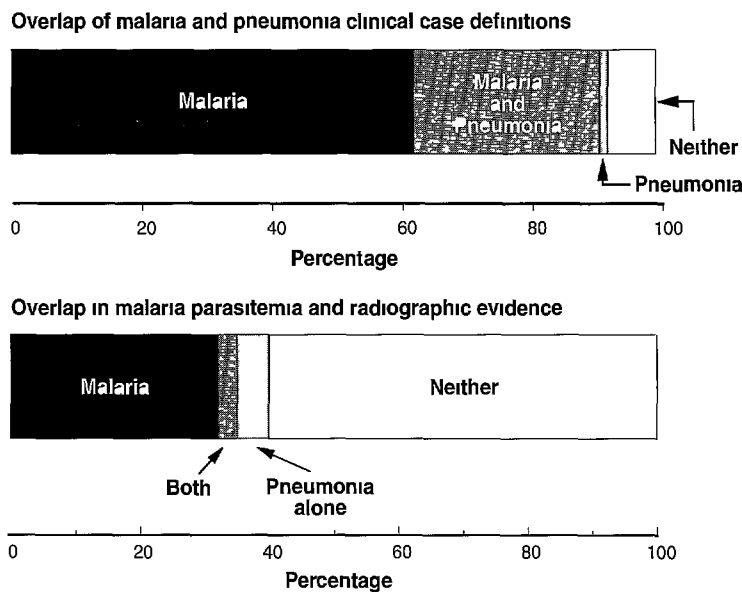
Malaria and ARI are the primary diagnoses for over half of the children seen as outpatients at health facilities in Malawi. A fraction of children with ARI have pneumonia and need treatment with an antimicrobial drug. A child with fever and cough may satisfy the clinical definitions for both malaria and pneumonia, but in a busy clinical setting be assessed and treated for only one. To determine the extent to which children who met the clinical definition for malaria also met the clinical definition for pneumonia (a subset of more severe ARI) a study was undertaken at the outpatient department of Kamuzu Central Hospital during a season of high incidence for both malaria and pneumonia (Redd et al. 1992).

**Study findings**

*Children who met the clinical and laboratory definitions* Of children brought to the hospital because of cough or fever and enrolled, 61% met only the clinical definition for malaria, 28% met the definition for malaria and pneumonia, and 1% met only the clinical definition for pneumonia. Almost every child that met the pneumonia case definition also met the malaria case definition (Figure 18).

*P. falciparum* parasitemia was detected in 35% of children and radiographic evidence of pneumonia was found in 8%. Of the children with radiographic evidence of pneumonia, 43/116 (37%) had coexisting *P. falciparum* parasitemia; the remainder were a parasitemic.

**Figure 18** Overlap of malaria and pneumonia clinical case definitions and malaria parasitemia and radiographic evidence of pneumonia



The clinical definitions and laboratory findings overlapped substantially. 95% of children meeting the clinical definition for pneumonia also met the clinical definition for malaria. Children with *P. falciparum* parasitemia were as likely to have radiographic evidence of pneumonia as those without parasitemia and were also as likely to have severe radiographic changes.

*Efficacy of cotrimoxazole* A 5 day course of cotrimoxazole at the standard dosage and duration recommended for treatment of pneumonia was assessed for antimalarial efficacy. All children that were followed for 14 days (96% of those enrolled) became a parasitemic at a mean of 2.7 days after the initiation of treatment with a mean fever clearance time of 1.5 days. Children remained parasite free for the 14 day follow up.

### **Impact on policy**

The results were used to emphasize the need for health workers to evaluate children with cough and fever for both pneumonia and malaria. The finding that cotrimoxazole was effective treatment for malaria in children permitted the National Malaria Control Program to recommend in the 1992 Treatment Guidelines that a child treated with cotrimoxazole need not receive an antimalarial.

## **III D 2 a (ii) Alternative clinical case definitions for malaria in children**

### **The question**

The second study assessed the existing clinical case definition used for presumptive therapy of malaria and assessed alternative clinical case definitions for the diagnosis of malaria in children at two sites: Mangochi District Hospital and Nkhoma Hospital.

### **Study findings**

*Reported history of fever* Nearly 90% of children were reported to have had a febrile illness by the mother and thus would have been treated presumptively for malaria, fewer than 40% had an elevated rectal temperature. The discrepancy may be due to mothers erroneously identifying many illnesses as having a fever component or to children with intermittent fevers being seen during a period when their temperature was normal.

*Sensitivity and specificity of clinical case definitions* In evaluating case definitions for malaria and defining malaria as *P. falciparum* infection of any density, the national policy was over 90% sensitive but only 21% specific (Table 6). The combination of rectal temperature  $\geq 37.7^\circ\text{C}$  or splenomegaly or nailbed pallor, three findings that were individually highly associated with parasitemia, was 85% sensitive and nearly 41% specific. Other findings and other combinations were either too insensitive or too nonspecific to be used to decide which children to treat for malaria.

**Table 6 Clinical case definitions to identify malaria parasitemia, wet season, Malawi, 1993**

Definition	Sensitivity* (%)	Specificity** (%)	Positive predictive value*** (%)
Any history of fever	93	21	63
Complaint of fever	73	36	63
Elevated rectal temperature	45	75	72
Elevated rectal temperature or splenomegaly	70	59	72
Elevated rectal temperature or splenomegaly or nailbed pallor	85	41	68

Sensitivity refers to the proportion of all children with parasitemia who would be identified using the given definition.

Specificity refers to the proportion of all children without parasitemia who would be identified by not meeting the given definition.

Positive predictive value refers to the proportion of children meeting the given definition who actually have parasitemia. This proportion may be affected dramatically by the prevalence of infection in the population.

This assessment of alternative case definitions suggests that a combination definition of objectively measured elevated temperature or enlarged spleen or pallor may be a better guide for antimalarial treatment than asking the mother if the child has had a fever. The slightly lower sensitivity of this combination definition means that some children with malaria parasitemia will not be identified. Most children not identified by these more restrictive definitions had lower density parasitemias and hemoglobin concentrations not in the anemic range and thus would be expected to do well without specific therapy for malaria. The advantages of a more restrictive definition are that fewer children who do not have parasitemia would be treated for malaria. This would result in substantial cost savings and would potentially delay the emergence of resistance to antimalarials such as SP.

### **Impact on policy**

The MOH is currently considering the results of this study and a possible follow-up study to evaluate the impact of a revised definition on the management of malaria and determine whether parasitemic children who are not clinically considered to have malaria by a more restrictive case definition will do well following discharge from the clinic without specific treatment for malaria.

## **III D 2 a (iii) Clinical versus laboratory diagnosis of malaria in adults**

### **The question**

The third study was conducted at QECH in Blantyre during the 1993 rainy season to compare the costs of performing microscopy on all adults with a recent fever history and treating only parasitemic persons with the costs of treating all adults with a history of fever for malaria (the current policy). The study was conducted in 1 week phases. During phase one, all adults with fever were treated with SP and microscopy was not performed. During phase two, all adults with fever had a blood smear and were treated with SP without the results of microscopy. During phase three, all adults with a history of fever had a blood smear and received treatment with SP only if malaria parasites were found.

### **Study findings**

*Use of SP and cost savings* The proportion of prescriptions for SP fell during each phase of the study, from 40% in phase one, to 21% in phase two, to 7% in phase three. The reduction of SP consumption during phase three would result in a savings at QECH outpatient department of \$17,430 per year. With an annual cost of \$3,980 for microscopy (two technicians, one phlebotomist, supplies, and stains), a change in policy that would require laboratory confirmation for the use of SP would produce a net savings of \$14,470 per year for this facility.

The results of this study are most applicable to hospitals where large numbers of patients are evaluated. The cost of a technician to perform the microscopy would be the same even if fewer smears were done, although fewer smears would reduce the potential savings. Furthermore, this study evaluated a strategy of limiting drug treatment in adults, in whom the health consequences of malaria are less severe than in children. The treatment dose of SP for adults is larger than it is for children although the costs of microscopy are the same, so applying this strategy among children would result in smaller cost savings than among adults.

### **Impact on policy**

The plans for refurbishing the outpatient department at QECH in 1994 include space for microscopists to interpret malaria smears. A final decision on how to incorporate microscopy into routine outpatient care had not been made as of September 1994.

### **III D 2 b Assessment of malaria vectors**

#### ***The questions***

The 1990–1994 National Malaria Control Plan included alternative control methods as a program element and outlined strategies for building capacity in this area, one of which was to better understand the characteristics of the malaria vector population, including its geographic and seasonal variations. The evaluation of malaria vectors was seen as a first step toward examining the potential for malaria prevention through personal protection (e.g., insecticide-impregnated bed nets) and highly selective vector control. As a consequence, from October 1991 through September 1992, an assessment of malaria vectors was carried out during four seasons in three geographically distinct districts.

#### ***Study findings***

Malawian vector assessment teams were trained, and MOH laboratory staff were taught laboratory skills to conduct field and laboratory evaluation of malaria vectors. In three districts (Dowa District at 1,120 meters above sea level, Mangochi District at the lake shore and 475 meters above sea level, and Nsanje District along the shores of the lower Shire river and 70 meters above sea level), village-based collections of malaria vectors were conducted at four times: October–November (dry season), January–February (early rainy season), April–May (late rainy season), and August–September (postrainy season). 1992 was a dry year, and the rainfall during the rainy season was approximately one-half of the average for these areas of the country. Vector abundance in households, biting rates, and sporozoite rates (proportion of vectors infected) were assessed.

*Vector abundance and biting and sporozoite rates.* *Anopheles gambiae s.l.* and *An. funestus*, important vectors of malaria elsewhere in sub-Saharan Africa, were found at all sites in numbers that varied by season and locality. The entomologic inoculation rate (EIR) (the number of infective bites/person/year) transmitted by both species combined was estimated at 16.22 in Dowa, 18.27 in Mangochi, and 1.16 in Nsanje. Because the assessment occurred in an unusually dry year, the actual average EIRs may be as much as 2-fold higher in each area. Vector abundance and biting and sporozoite rates varied by season, with the highest seasonal EIRs seen in Dowa and Mangochi during the rainy and postrainy seasons. However, during the dry season, EIRs were lower and remained moderate along the lakeshore and lower Shire Valley (Mangochi–Nsanje) but nearly undetectable on the plateau (Dowa).

#### ***Impact on policy***

These studies trained a cadre of workers in malaria vector assessment techniques and demonstrated that the major malaria vectors in Malawi are indoor-biting, indoor-resting species that bite primarily during sleeping hours. The studies also showed that vector abundance and biting and sporozoite rates varied by season and location in the country (lakeshore and Shire river valley versus plateau). Thus, the use of insecticide-impregnated bed nets will likely reduce transmission of malaria because they are particularly suited to prevent indoor biting during sleeping hours. The transmission reduction that may be achieved by this control measure requires further evaluation because the expected 80% reduction in transmission seen in other studies may still leave EIRs at greater than 5 infective bites per person per year and therefore may not actually alter infection and illness rates in the at-risk populations in Malawi.



### III D 2 c Economic cost of malaria

#### ***The questions***

The National Malaria Control Committee recognized that knowledge of the economic impact of malaria was needed to set realistic research and program priorities to improve malaria control program management. Although the health burden of malaria was known, no data existed on the economic burden of malaria in Malawi for households, the health care system, and the national economy. In 1992 a series of interrelated investigations was conducted to collect such data. There were three parts: 1) a nationwide household KAP survey which included questions on household expenditures for malaria and time lost to malaria illness; 2) interviews of patients with malaria at selected outpatient and inpatient facilities; and 3) a retrospective hospital medical records review. During the KAP survey 1 531 heads of households were questioned. Over 1 000 malaria patients were interviewed in the facilities survey; approximately 8,500 inpatient hospital medical records were reviewed.

#### ***Study findings***

*Household income* At the time of the survey, median income per household was \$155<sup>8</sup>. Very low income households with an average annual income of \$68 earned primarily (92%) through farm production, represented 52% of the households surveyed.

*Direct costs* Only 10% of all households and 4% of very low income households reported any expenditures related to malaria prevention. However, all households reported some expenditure for malaria treatment. Malaria illness was common, with seasonally adjusted annualized estimates of 7.5 fever (malaria) episodes in children less than 10 years of age and 6.1 episodes in adults. Total annualized expenditure per household of four for malaria episodes was \$19.83, or 4% of mean household annual income. Among very low income households, expenditure was \$19.13, or 28% of mean annual household income.

Malaria accounted for 34% of outpatient visits and 15%–35% of all hospital admissions. The annual cost to the health care system for the treatment of over 1.1 million outpatient malaria cases was estimated to be \$1.3 million—\$821,000 at MOH facilities and the remainder at mission and other private facilities. Direct costs per malaria case at MOH and PHAM hospitals were \$49 and \$22, respectively. The total direct cost of inpatient malaria treatment borne by the MOH was \$1.4 million, or 5.4% of the annual MOH budget.

*Indirect costs* The value of time lost in caring for children with malaria was estimated to be \$18–28 per household per year on the basis of the number of malaria episodes per child and the days of work lost per malaria episode in a child. The value of time lost due to adult malaria was estimated to be \$4–\$5 per adult per year, giving a total annual indirect cost of productive time lost of \$35–\$44 million per year in Malawi (Table 7). In addition, results from previous studies estimating age-specific malaria mortality rates in Malawi showed that the cost of premature mortality was estimated to be \$63 million per year.

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<sup>8</sup> Conversion rate (1992): 3 Malawi kwacha = U.S. \$1.00

**Table 7 Direct and indirect household costs of malaria in Malawi, 1992**

	All households \$ (% of annual income)	Very low income households \$ (% of annual income)	Low to high income households \$ (% of annual income)
Direct treatment	19 83 (4 1)	19 13 (28)	19 94 (21)
Direct prevention	2 55 (0 5)	0 59 (0 9)	4 70 (0 5)
Indirect costs	12 75 (2 6)	2 13 (3 1)	20 61 (22)
<b>Total costs</b>	<b>35 13 (7 2)</b>	<b>21 85 (32)</b>	<b>45 25 (4 7)</b>

### ***Impact on policy***

This investigation provided the first data on the direct and indirect costs associated with malaria prevention and treatment in Malawi. Malaria represents a significant burden to the national health sector and household economies; this finding provides added support for Malawi's renewed efforts and investment in its malaria control program. The information obtained from the economic studies can be used to develop health education messages that will help households combat malaria most economically. Such information can also be useful to policy makers considering health financing strategies for Malawi's health care system. Information on the economic impact of malaria is essential to donors and others interested in the economic burden of disease and decisions about priority setting in resource allocation.

## **III D 3 Studies of malaria interventions**

### **III D 3 a Definition of parameters for evaluating drug efficacy**

#### ***The questions***

With the increase in childhood morbidity and mortality due to anemia—often directly caused by malaria—and concern that CQ resistance had intensified, the current efficacy of the first-line antimalarial CQ needed to be assessed parasitologically, clinically, and hematologically. In addition, parameters with which to judge the efficacy of any antimalarial needed to be defined. In 1990 at Karonga District Hospital and in a subsequent follow-up study in Mangochi, children less than 5 years of age with signs, symptoms, and laboratory documentation of malaria were treated with either CQ 25 mg base/kg over 3 days or SP of the WHO recommended standard dosing for age groups. Parasitologic, clinical, and hematologic responses were measured.

**Study findings**

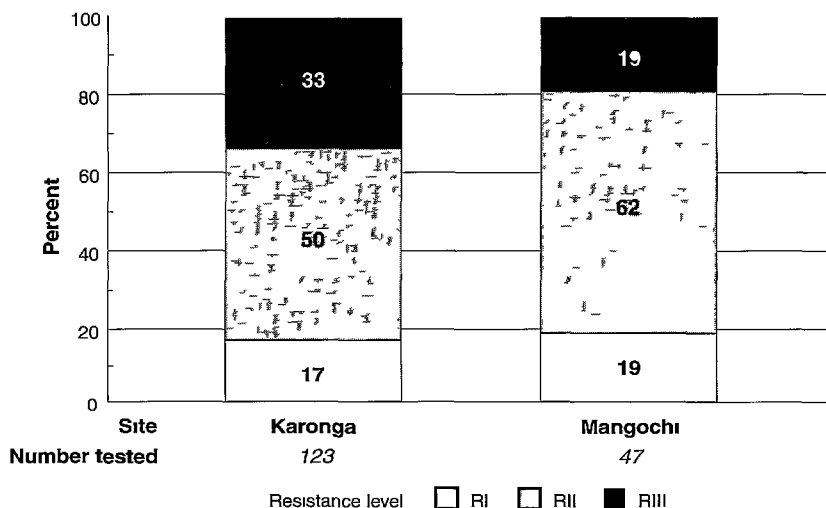
**Box 8. Clinical, hematologic, and parasitologic measures of antimalarial efficacy**

On the basis of studies conducted initially in Malawi, it is now accepted that the efficacy of an antimalarial used to treat children less than 5 years of age (those at highest risk for severe illness and death from malaria) can best be judged by a combination of the antimalarial's ability to alleviate symptoms of the disease, clear parasites and allow an adequate parasite free interval for hematologic recovery (defined as the return to pre-illness level of hemoglobin concentration) (Bloland et al 1993). Studies in Malawi from 1984 through 1991 demonstrated that parasite resistance to CQ intensified both in overall prevalence of resistant parasites and in the proportion of RIII resistant parasites. Chloroquine's subsequent failure to clear peripheral parasitemia resulted in shortened duration of clinical improvement and inadequate recovery from the associated anemia. Collaborators in Malawi agreed that it was time to change to a drug that would clear parasitemia when treatment resulted in the following: a mean sustained clinical recovery less than 14 days and a mean hemoglobin concentration increase among anemic children (<8 g/dL initially) of less than or equal to 1 g/dL within 14–21 days. Experience in Malawi suggested that these events occur in proportion to the frequency of high level resistance, when RIII infections account for more than 5%–10% of infections, these clinical and hematologic problems will be observed. In older individuals (those at less risk of malaria morbidity and mortality), the requirement for parasite clearance may be less critical.

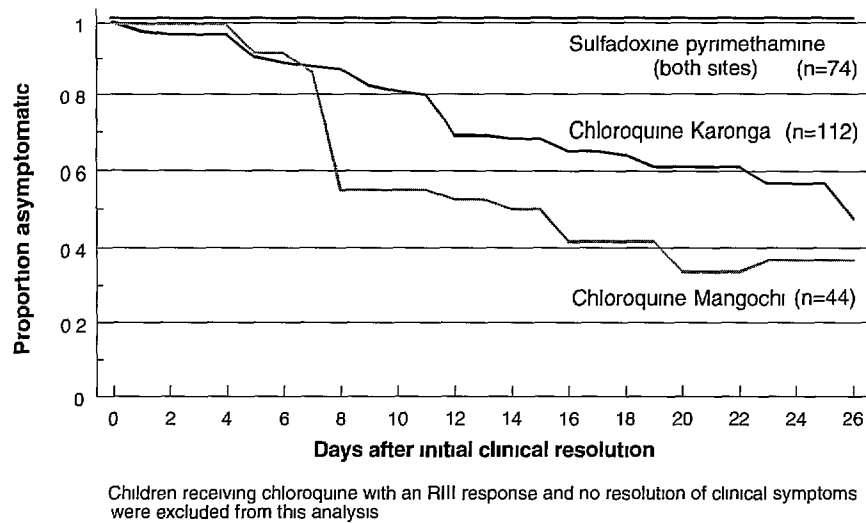
The recognition of clinical and hematologic effects of parasite resistance was critical in making the decision to change the national policy in Malawi. These requirements are being adopted elsewhere (e.g. Kenya, the World Health Organization) as decision points for planning malaria treatment guidelines.

*Parasitologic and clinical response to CQ* This study found that more than 90% of children treated with CQ remained parasitemic; most resistance patterns were RII or RIII (Bloland et al 1993) (Figure 19). Despite this high level of resistance, 78% of children treated with CQ became afebrile and had normal activity levels within the first 48 to 72 hours after therapy. In children who responded clinically, 37% had recrudescence signs of malaria within 14 days after therapy and 58% had signs by 28 days after therapy. Children with an RIII pattern of resistance failed sooner than children with an RII pattern. In addition, although approximately 80% of children treated with CQ achieved rapid resolution of fever and improved clinically, the median duration of the clinical improvement after CQ therapy was under 2 weeks. A follow-up study conducted in Mangochi in 1991 showed a very similar pattern of clinical failure after CQ therapy, further supporting the findings of the study (Figure 20).

**Figure 19 In vivo chloroquine resistance profiles by site, Karonga (1990) and Mangochi (1991)**



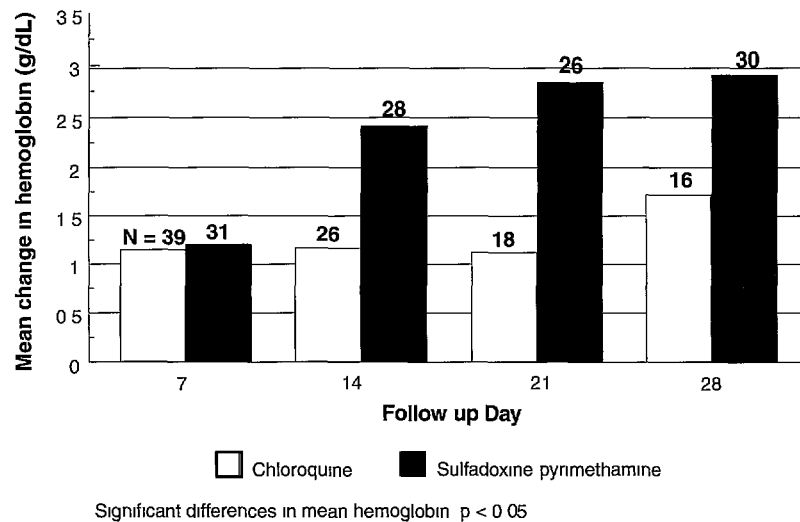
**Figure 20 Time from clinical improvement to clinical failure for children less than 5 years of age treated with chloroquine or sulfadoxine-pyrimethamine, Malawi, 1990-1991**



These levels of resistance compare with findings from a 1985 study demonstrating that although about 50% of children remained parasitemic 1 week after CQ therapy, over 90% became afebrile within 72 hours of CQ treatment. In later studies, although there was a higher degree of parasitologic resistance, the rate of initial clinical response was similar (78% v 90%) but 58% eventually failed clinically (Pappaioanou et al 1988). By 1990-1991, an increasing number of early parasitologic and clinical failures was observed (Bloland et al 1991a).

*Hematologic response to CQ and SP* Hematologic improvement (increasing hemoglobin concentration or increasing packed red blood cell volume) after treatment was also examined in the studies conducted in 1990 and 1991. The finding that hematologic response to CQ was inferior to that after SP treatment was attributed to increasing CQ resistance. CQ resistance had become high enough to prevent children from achieving acceptable hematologic recovery (Bloland et al 1991a). In comparison, children who were treated with SP, a drug that reliably cleared parasites, remained free of clinical symptoms and had significantly greater increases in hemoglobin concentration over the follow-up period (Figure 21).

Figure 21 Mean hemoglobin change after therapy with chloroquine or sulfadoxine-pyrimethamine, Malawi, 1991



### Impact on policy

Because treatment with CQ failed to produce either lasting clinical improvement or adequate hematologic recovery CQ could no longer be considered adequate therapy of clinical *P. falciparum* malaria in Malawi's children (Box 8). In the treatment guidelines of 1992, regimens using SP replaced those using CQ for treating very young children and for chemoprophylaxis of pregnant women (see III D 2 b) (Box 9). The guidelines cited not only its greater efficacy, but its increased likelihood of compliance (single dose required, tasteless), limited side effects, and low cost (comparable to CQ). The policy was implemented in March 1993 when sufficient quantities of SP were made available.

### **Box 9 A critical step Changing first-line therapy**

Because of the importance of effective treatment and because of research results in 1990 and 1991 efforts from 1991 through 1993 were invested in revising the national policy to incorporate the change from chloroquine (CQ) to sulfadoxine pyrimethamine (SP) as the first line drug. The steps Malawi took to initiate and implement this change are described below.

- An October 1991 national meeting in Mangochi reviewed recent study results and revised malaria treatment guidelines which were updated again in November 1992 and printed. The revised guidelines of 1992 reflected three changes from the 1986 guidelines: SP replaced CQ as the first line drug for treatment of malaria in young children and for chemoprophylaxis for pregnant women. It was also recommended that a patient treated with cotrimoxazole for a bacterial infection (e.g. chest infection) should not also be given an antimalarial because cotrimoxazole would also treat malaria. The National Drug Committee discontinued AQ as a recommended second line drug due to concerns about serious side effects and its limited benefit with the high level of CQ resistance in Malawi.
- In early 1992, to further the implementation of the change in drug policy a meeting was held with representatives of private sector pharmaceutical companies to encourage them to procure SP at the same time they allowed the stock of CQ to decline. The officer in charge of the Central Medical Stores (the government agency responsible for national drug procurement) had participated in the discussions that led to the replacement of CQ as the first line drug. By March 1993 the Central Medical Stores had purchased and distributed sufficient amounts of SP for use in the health delivery system.
- In November 1992 the Malaria Control Program organized the Information Education Communication materials development workshop, which had multisectoral representation — personnel from the government, nongovernmental organizations, clinicians, and others involved in the health delivery system. Treatment guidelines were finalized, the 1985 treatment chart was revised, radio messages were developed, and seven posters were designed. In September 1993, another workshop was held to develop materials that would help counter people's perception that SP was not effective. Oral reports of an influenza outbreak in the country provided a possible explanation for the lack of confidence in SP. The treatment chart was modified to include paracetamol in addition to SP. The workshop also prepared material for newspapers and radio (poems, stories, jingles, and dramas), comics for school use, and charts of the life cycle of the mosquito and malaria parasite. The posters developed at the 1992 meeting were modified and six others were designed.
- Prior to the March 15, 1993 official launching of the change from CQ to SP, regional meetings were held in December 1992 and January 1993 to inform district health management teams composed of district health officers, matrons (nursing supervisors), district health inspectors, and pharmaceutical assistants of the change. These teams in turn briefed other health workers in their district. Another briefing was held for malaria control coordinators who were in charge of notifying community level health providers (traditional birth attendants, health surveillance assistants, village health workers, and shopkeepers) of the change. By the end of 1993 all health workers had been informed.
- For the official launching of the change to SP as the first line drug, the Minister of Health invited other Ministry heads and the press to headquarters for his address to the nation. The Secretary of Health had requested that hospitals have enough SP to begin distribution in March, and the Ministry of Health provided financial assistance to hospitals for purchase of the drug.
- After the introduction of SP, forms designed to track drug availability, resistance, and adverse side effects were distributed to district health officers who were then responsible for returning them to the Malaria Control Program's office in Lilongwe.
- Refresher training was conducted for sentinel surveillance personnel, instructing them in the new policy, the use of the new data collection forms, and new health education materials.

### III D 3 b Effective regimen for preventing malaria during pregnancy

#### The questions

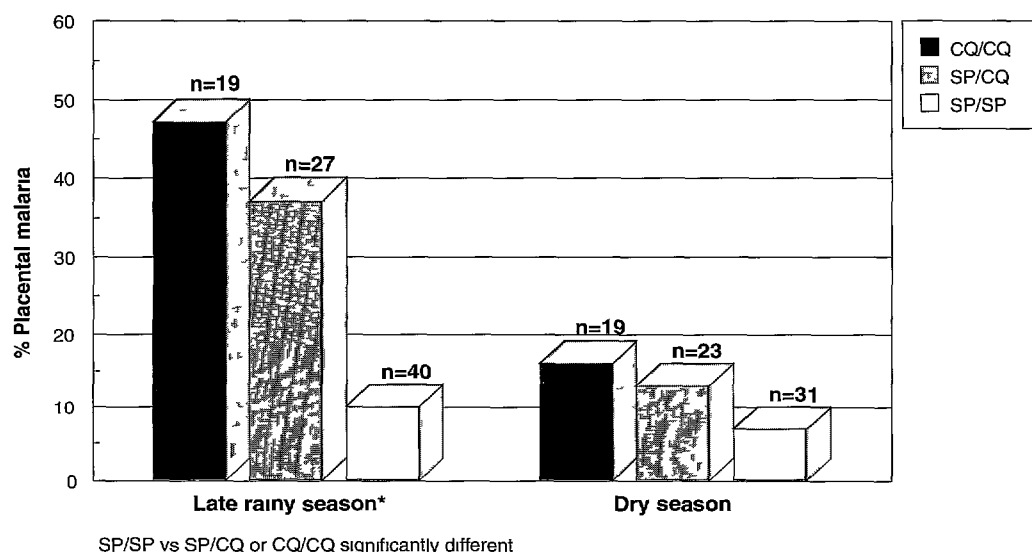
With the knowledge that an efficacious antimalarial delivered to women in their first and second pregnancies could prevent a significant amount of LBW (Steketee et al 1993d) the National Malaria Control Committee decided that prevention of malaria during pregnancy was a critical issue in child survival that warranted further investigation. To develop guidelines for maternal malaria control, the committee needed to identify an effective, practical antimalarial regimen. A study conducted in Mangochi District during 1992 compared the efficacy in preventing placental malaria, cost and cost effectiveness of three regimens for women in their first or second pregnancies.

- 1) CQ/CQ CQ treatment (25 mg base/kg over 3 days) at initial ANC visit (usually in the middle of the second trimester), followed by CQ weekly (300 mg base), which previous studies had demonstrated to be slightly more effective than the current recommended regimen of CQ weekly with no initial treatment dose (Steketee et al 1993d)
- 2) SP/CQ SP treatment at the initial ANC visit to clear parasitemia initially followed by weekly CQ prophylaxis to decrease the amount or occurrence of parasitemia
- 3) SP/SP SP treatment at the initial ANC visit followed by a second treatment dose of SP at the beginning of third trimester, which would clear parasitemia initially and again at the time of maximal fetal growth

#### Study findings

*Efficacy of candidate regimens* At their ANC visit, approximately 65% of women in their first or second pregnancy had peripheral parasitemia (Schultz et al 1994d). At least 24% of women receiving CQ/CQ had peripheral parasitemia throughout pregnancy, while fewer than 5% of the women receiving SP/SP were parasitemic at follow up assessments (Figure 22). At delivery, the group receiving SP/SP had significantly lower rates of peripheral (3% versus 32%) and placental (9% versus 32%) parasitemia than women receiving CQ/CQ. The difference in the efficacy of the regimens was even more striking among women delivering during the high transmission season.

**Figure 22 Placental parasitemia among pregnant women receiving antimalarial regimens, Mangochi, 1992**



*Economic comparison of candidate regimens* A decision analysis model was used to estimate the cost effectiveness of the candidate regimens when delivered to women in their first or second pregnancy (Schultz et al 1994c) Given current levels of ANC attendance compliance with dispensed antimalarials costs of antimalarials and efficacy of the antimalarial regimens the cost-effectiveness of the regimens (cost per case of LBW prevented) for SP/SP, SP/CQ and CQ/CQ was estimated to be \$9 66 \$59 and \$113 respectively The cost effectiveness of these regimens depended largely on the price of the antimalarials the number of weeks of CQ prophylaxis drug efficacy and compliance

### ***Impact on policy***

In October 1992 results of this study were presented at the National Malaria Control Committee meeting On the basis of the need for maternal malaria control and the identification of an efficacious and practical antimalarial regimen the SP/SP regimen was adopted as the recommended regimen for pregnant women As outlined in the study the regimen required that women attending ANC be given one treatment dose of SP during the second trimester (usually the first ANC visit) followed by a second dose at the beginning of the third trimester The regimen was recommended for women who were at least 16 weeks pregnant and excluded women with a history of sulfa allergy

## **III D 4 Studies of malaria treatment and prevention practices**

### **III D 4 a Knowledge, attitudes, and practices malaria in children and pregnant women**

#### ***The questions***

The design of effective new health education messages resulting from the change in the first line antimalarial required an understanding of case management of febrile illness in children in the community The design and implementation of malaria prevention strategies delivered through ANC also required information regarding women's use of ANC and their perceptions of malaria during pregnancy Furthermore baseline data about malaria treatment and prevention were needed for subsequent monitoring and evaluation of policy and program changes This information, along with information on general knowledge of malaria illness malaria prevention and household expenditures on malaria was collected in the spring of 1992 during a nationwide malaria KAP survey (Steketee 1994)

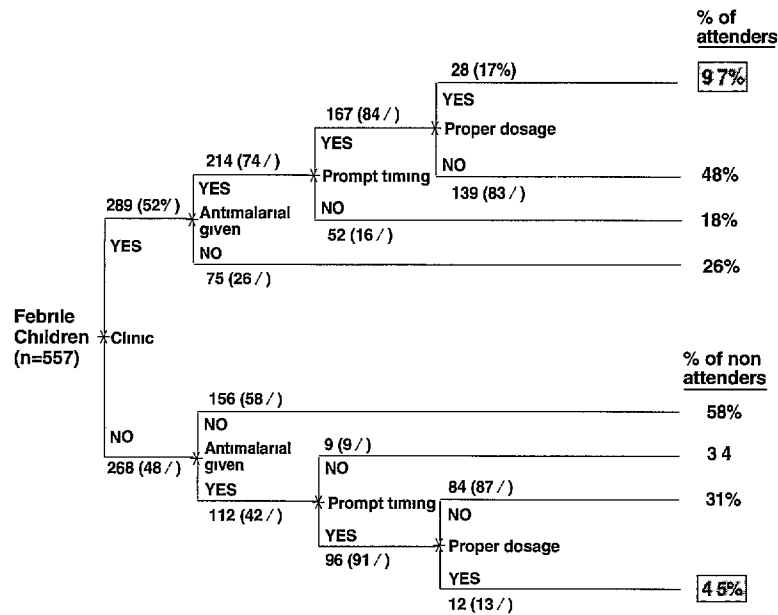
#### ***Study findings***

*General malaria knowledge* The KAP survey found that although malaria is commonly reported and perceived to be a very important health problem both for children and for pregnant women knowledge of malaria and its effects was generally limited and often erroneous (Ziba et al 1994) For example slightly more than half of the heads of household (55%) knew that malaria was transmitted by mosquito bite 19% believed cold weather to be responsible People's information about malaria was obtained from a variety of sources including health clinics, the radio, and other people

*Management of febrile illness in children* Only 52% of caretakers took their febrile child to a clinic for diagnosis and treatment These children were more likely to receive antimalarials than children who were not taken to a clinic (Slutsker et al 1994) Still only 74% of clinic attenders reported being administered an antimalarial, compared with 42% of nonattenders Overall fewer than 10% of febrile children received prompt (within 2 days of fever onset) treatment with a full dosage of the recommended antimalarial (Figure 23)



Figure 23 Reported treatment of febrile illness in children, national survey, Malawi, 1992



Beliefs and practices about malaria prevention during pregnancy The majority of recently pregnant women, more than 90% of whom had attended ANC during their previous pregnancy, perceived malaria as a health problem during pregnancy (Schultz et al 1994b) Though most women attended ANC, where they were given CQ prophylaxis to take weekly only 69% of women believed that antimalarials were effective in preventing malaria Further more, 36% of women thought that antimalarials were potentially harmful to a pregnant woman or her unborn child

Household prevention measures A little over half (52%) of the respondents reported using malaria prevention measures in their households (Ziba et al 1994) (Table 8) Among users 47% reported use of purchased products while 64% used naturally available products Use of a purchased product for malaria prevention was strongly associated with an increasing education level of the head of household and an increasing household income level

Table 8 Reported use of household prevention measures, national survey, Malawi, 1992

Prevention measure	Number of households	(%)
Purchased		
Mosquito coils	238	(16)
Insecticide spray	171	(11)
Bednets	99	(7)
Repellent	12	(1)
Not purchased		
Burn leaves/herbs	271	(18)
Burn spread/dung	109	(7)
Fire in house	206	(14)

***Impact on policy***

Data gathered in the KAP survey provided malaria control policy makers with important information to be used in designing and evaluating the success of health education messages aimed at increasing general awareness of malaria, prompt and proper treatment of febrile illness in children and antimalarial coverage among pregnant women. These baseline data will be invaluable for monitoring and evaluating the effects of the changeover to SP for both treatment among young children and prevention among pregnant women.

### III E Impact of studies on policy a summary

From 1990 through 1993, data collected and analyzed, principally from a series of field studies but also from national HIS sources, provided needed information for revisions of policy, planning, and national guidelines for malaria control. These were summarized in the previous section, important points are highlighted below.

*The problem of malaria* Several studies addressed three of the elements of the 1990-1994 National Plan for Malaria Control (improved understanding of malaria, accurate diagnosis, and alternative methods of control). The study of the overlapping diagnoses of malaria and pneumonia led to the recommendation in the 1992 Treatment Guidelines that a child treated with cotrimoxazole, typically a drug prescribed for pneumonia, need not also be given an antimalarial, as cotrimoxazole was effective treatment for malaria. Additional studies of diagnostic criteria for malaria (clinical and/or laboratory) have led to heightened awareness of the diagnostic problems posed by the disease and may lead to wider use of microscopy and the incorporation of several clinical criteria beyond "history of fever" into the presumptive diagnosis. Studies of malaria vectors in Malawi have improved the understanding of the potential for personal protection measures (e.g., insecticide-impregnated bed nets) as a transmission reduction strategy. Both the MOH and the private sector are interested in insecticide-impregnated bed net programs. Finally, economic assessment studies demonstrated that malaria represents a major economic burden to families and to the nation. The current level of support from the MOH and the donor community reflects the recognition of this problem. The methods used to collect these data in Malawi represent a standard that should be considered for similar future studies of malaria or other diseases in Malawi or elsewhere in the region.

*Malaria interventions* Two elements of the 1990-1994 National Plan (effective treatment and effective prevention in high-risk groups) were addressed. Studies to evaluate the efficacy of CQ using parasitologic, clinical, and hematologic outcomes led to the replacement of CQ with SP in the 1992 Treatment Guidelines, the policy was implemented in 1993 when sufficient quantities of SP were available. WHO is currently considering adopting the methodology developed during these studies for standard use when evaluating drug efficacy and selecting alternative antimalarial drugs for primary therapy of uncomplicated illness. On the basis of studies evaluating the efficacy and cost of CQ and SP regimens for the management or prevention of malaria during pregnancy, the national guidelines were modified to recommend SP in a two-dose intermittent treatment regimen for pregnant women. Similarly, this methodology for examining prevention in pregnancy is being considered for use in other parts of Africa to refine treatment and prevention policies for pregnant women.

*Malaria practices* Several elements of the 1990-1994 National Plan (improved understanding, effective management, and increased GOM and donor investment) were addressed by efforts to better understand malaria-related practices in Malawi. Data from a KAP survey were critical for the design of health education messages for malaria prevention and control. Also, the KAP survey provided a baseline for current practices, with the change of first-line therapy to SP, further surveys can monitor and evaluate its effects. Finally, linking the KAP study to the economic study allowed for a household assessment of the impact of malaria in Malawi and provided evidence of the widespread adverse health and economic impact that malaria has on Malawian families.

In addition to the above-mentioned impact of studies on policy and program development, there was tangible evidence of increased GOM support of malaria control in Malawi during the early 1990s. The national level and district level staffing for malaria control was increased, and several staff were enrolled in postgraduate programs that emphasized public health, epidemiology, and malaria control.

The research capacity has been generally strengthened with medical student involvement planned, continued involvement of the drug efficacy team, and a newly trained team capable of vector assessment studies

During the years 1990 through 1993, important lessons were learned

- The systematic approach toward policy, strategy, and guideline development has continued to be essential for orderly development and growth of the National Malaria Control Program Development has been even more systematized under the 1990-1994 National Plan with its 10 elements for action and the activities conducted subsequently to address these elements
- The decision to change the first-line drug in Malawi from CQ to SP was a major policy and program hurdle that could not have been considered without both data collected over time and analyzed in conjunction with key decision makers and the understanding and willingness to confront the steps of national consensus, pharmaceutical group involvement, and the participation of national-, regional- and district-level personnel responsible for health education, training, supervision, procurement, and distribution
- The decisions to modify the prevention strategy for pregnant women succeeded by employing the same process as described in #2
- Programmatic investment in insecticide-impregnated bed nets is now possible because of the understanding gained from studies conducted in representative areas of the country
- Increased national and donor commitment requires both data and constant attention from program staff, but it can be achieved, as the increased staff and modest supply and equipment resources that the Malawi program has obtained attest
- Although it has been easy to recognize that training, supervision, health education, and other elements of program support need strengthening, these remain difficult areas to affect and are often the last to receive attention and substantive resources

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## CHAPTER IV

# Malaria Control Investment in Malawi: A National Commitment and a Valuable Regional Experience

Lessons learned in Malawi in the areas of operational research and policy and program development may help others plan more efficiently the needed steps toward malaria control. Operational research conducted in Malawi has considerably expanded the technical database about malaria and effective control interventions in endemic areas of sub-Saharan Africa (Box 10). Study findings have set the standard for work remaining to be done in the region.

The relevance of the Malawi experience extends beyond providing operational research standards—Malawi has also explored the requirements for policy and program development for malaria control. The critical feature of Malawi's process has been its strong national commitment to developing an effective malaria control program. With this commitment, it involved key decision makers and identified people capable of conducting operational research who could identify the most important technical or programmatic obstacles, assess the issues through research and apply new-found information to improving the control program's effectiveness and efficiency. A policy embracing regular monitoring and evaluation of its program planning and implementation outcomes constitutes the model required for effective disease control programming. Malawi made great strides in developing such a malaria control program.

Several elements of malaria control development in Malawi should be highlighted. While these may not be models for other countries, they represent lessons for others to consider as they examine their own policy development process.

### IV A Components of Malawi's success

#### **The study of technical issues served as an entry point for engagement and continued involvement of key participants**

This document described the process of conducting operational research—examining study results and making decisions based on locally collected information. While this process has been central to policy, planning, and program development, it has also engaged junior MOH staff (clinicians, nurses, public health staff, and other decision makers) and university staff and students. By obtaining skills needed to gather data and to apply results to policy and program issues, staff and students have strengthened their ability to contribute to the malaria control program.

The operational research activities engaged a variety of health care professionals, including physicians, who retain much of the decision-making power within the health sector. Physicians involved in these activities were encouraged to seek the relevance of their research to the malaria control program. Clinicians participated directly in evaluating determinants of antimalarial drug efficacy, in drug efficacy monitoring, and in examining diagnostic criteria for malaria and other diseases with overlapping symptoms (acute respiratory infection). From this engagement, clinicians further recognized the role and determinants of patient participation in effective malaria control. Subsequently, clinicians reviewed the

### Box 10 Standards set for operational research in Africa

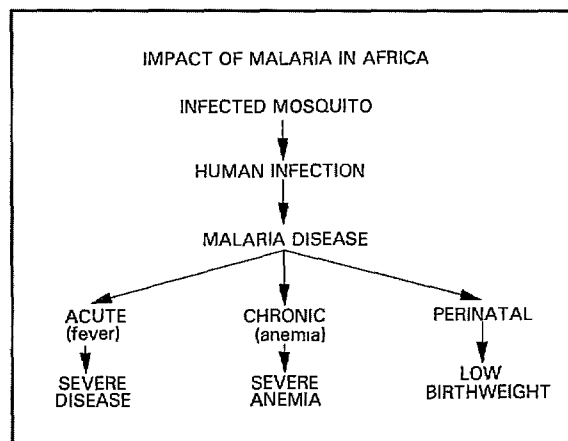
First Malawi provides the model to be followed for in vivo drug sensitivity testing and monitoring to develop the database for drug change. The modified version of the standardized WHO in vivo testing methodology that Malawi used proved to be fast, accurate, and feasible. Survey teams using this procedure obtained information on parasitologic, clinical, and hematologic response on which to base policy. One of the outcomes of this work was the understanding that large, widespread frequent antimalarial drug sensitivity studies do not need to be conducted, rather it is more important to obtain repeated data in selected areas representative of the country's geography. Applying this lesson could reduce markedly the time needed to assess patterns of resistance to antimalarial drugs.

The MMRP and other studies evaluated the problem of malaria infection in pregnancy. They provided the needed data to support the selection of the target group (primigravidas and secundigravidas) and the need for prevention of infection rather than only treatment of symptomatic malaria in these areas of high transmission typical of sub-Saharan Africa. Effective interventions were designed, one of which promises to be especially well-suited for inclusion in a program of antenatal health care: intermittent (twice during pregnancy) treatment with a highly efficacious antimalarial, SP. The effect of the mother's malaria infection on the child was fully explored, this work outlined the questions that need to be answered in other epidemiologic settings before effective programs are designed.

Malawi gathered baseline data regarding the current state of malaria knowledge, attitudes, and practices and the economic impact of the disease. Not only were these studies important in outlining a methodology to follow, but also in emphasizing the importance of determining baseline information. Even without a formally constituted national malaria control program, activities directly impacting malaria control programs are carried out in the community: Mothers, caretakers, and community volunteers diagnose children's fever and then provide treatment. Those who would like to, and can afford to, purchase sprays, nets, and other items in order to prevent the initial infection. Malawi's experience is that understanding the backdrop within which programs exist is essential to formulating programs that are efficacious, effective, and efficient.

The extensive work conducted to define the problem of severe malaria and to formulate interventions to manage this often fatal form of the disease has allowed patient evaluation standards and treatment guidelines to be developed. Other countries can adapt these to their own situations.

Finally, through continued internal and international collaboration in Malawi, investigators have clarified the modes of impact of malaria infection and disease (see figure). Malariaologists have come to understand that the control of malaria infection and illness must approach each of the aspects of the protean nature of the parasite and its effects: preventing infection from the mosquito, preventing the progression from infection to disease, managing acute uncomplicated and severe illness, managing or preventing the more silent forms of 'asymptomatic' infection (e.g., anemia) and preventing and managing the perinatal impact of infection and its associated illness in the pregnant woman or the consequence of low birth weight in the newborn.



KAP data, along with health education and public health specialists, to help focus malaria control programming efforts. Clinicians also recognized the need to evaluate the economic impact of malaria and of disease control efforts in the context of economic limitations as an important step toward allocating resources and creating a program relevant to patient needs and means.

Technical issues that are highlighted in the document include

- Results of drug efficacy studies leading to changes in malaria treatment guidelines
- Results of studies in malaria in pregnancy leading to changes in prevention guidelines
- Knowledge, attitudes, and practices (KAP) survey results leading to health education material design,
- Results for an economic study focusing donor and MOH attention to malaria issues, and
- Studies of severe and complicated malaria providing information for improved treatment guidelines

### **Focused operational research supported malaria program development**

The contribution of operational research to program development has not been adequately understood or supported. However, the experience in Malawi demonstrates the value of a partnership between program-relevant research and program development, in which focused scientific thinking supported and promoted program development.

In the evolution of the initial antimalarial drug efficacy studies and the subsequent studies to monitor drug efficacy, investigators in Malawi were faced with the question 'how will we know when the antimalarial drug is no longer effective?' This question was answered by defining the parameters of effectiveness (i.e., to resolve malaria-associated illness for a sufficient length of time to permit full recovery of the child [including hematologic recovery]) and then by developing a scientific study to examine whether the drug accomplished these requirements. Through this process, the information collected became directly relevant to the program's decision of when to change the first-line antimalarial drug.

Another example of the partnership of research and program development is the MMRP. This project was developed to answer a specific set of questions regarding whether or not a highly effective antimalarial drug used for prevention of malaria in pregnancy would lead to a reduction in the frequency of LBW in the population. This population-based research program led to an answer to this question of regional importance, and at the same time, results of the study led the MOH to seek an effective, affordable, and safe regimen that could be promoted for malaria prevention in pregnancy. In addition, important observations on malaria in pregnant women and their infants were made. The research fostered an ongoing collaboration between Malawian and U.S.-based malaria experts that continued to support systematic approaches to policy and program development.

While operational research served many important purposes in Malawi, the operational research described in Malawi is not meant to be a recipe for all such studies to be conducted in each malaria-endemic country in sub-Saharan Africa. In fact, it is hoped that information dissemination will play an increasing role so that relevant information from one country might be examined critically and adopted as appropriate to the local circumstances in another country in the same region. For example, a large-scale longitudinal study of malaria prevention in pregnancy like the MMRP need not be repeated in each country. Efforts are currently under way to develop simpler rapid assessment tools that can provide relevant information within a country. These tools should facilitate the adoption of the broad principles of malaria prevention in pregnancy and help tailor the program to local needs.

**The development of the malaria control infrastructure and management capacity is best addressed by training**

Although much remains to be done within Malawi in infrastructure and management development the MOH has made a substantial effort to include staff in a variety of categories and levels provide training and offer young staff leadership opportunities Malawi's malaria program has been built on the recognition that increasing management capacity required both short- and long-term investment in training

The ultimate sustainability of the malaria program or any other disease control program will be its ability to entice people to participate to support them, to show progress and to reward them for work well done Malawi's program has contributed on these fronts largely through the recognition by a few that these issues were important for the sustained nature of the effort Clinical officers were brought into the decision making role laboratorians were involved on a co-equal basis and additional staff were trained in malaria control issues on their return from study abroad

The control of malaria in Malawi is a dynamic, ongoing process The investments to date in identifying the control challenges and effective control interventions and in nurturing a competent national staff have been essential initial steps Continued investments in these areas will be required as national attention moves to wider application of the control strategies increasing coverage and access of the Malawian population to malaria control services Distinct challenges remain that will require continued support and innovation to ensure that Malawi's malaria control program is effective

## **IV B Challenges to be addressed**

**Ensuring adequate resources for malaria control** As with almost all disease control programs in developing countries the malaria control program in Malawi has been faced with a limited MOH budget and continued requirements for donor assistance While budget limitations have not jeopardized the control program to date they have limited the planning capability and accomplishments by the national program Recent data from the economic evaluation of the cost of malaria to the country and its people provide important documentation of need the MOH and donors must weigh this need against other needs within the health sector

**Continued attention to develop the malaria control infrastructure** The small staff (both technical and administrative) and inadequate central resources (e.g. vehicles) for the National Malaria Control Program also limit the capabilities of the program to provide regional and district level guidance, supervision, training, and other services

**Development of program management and administrative capacity** As is the case throughout the MOH, the staff of the malaria control program have little or no training or experience in management and supervision This situation is unlikely to change except as improvements occur more widely within the MOH Additional efforts to train potential leaders in these skills will need to be considered

**Ensuring sustainability in malaria control programming** Like other disease control programs the National Malaria Control Program faces the continual question of adequate staff and resources to carry out its mission Recent efforts to train junior staff will undoubtedly foster the sustainability of the program



## **IV C Malawi's experience and the Global Strategy for Malaria Control**

Malawi's process of policy and program development was initially approached as a linear set of actions. Defining effective malaria control interventions was based on operational research designed to address a perceived lack of information. The results led to policy definition, which was elaborated in malaria control plans and treatment guidelines. The plans were then implemented and evaluated. An implicit assumption in the early stages of the malaria control activities was that few malaria control actions were in place and that the national initiative would need to define policy and develop program infrastructure in total.

This implicit assumption was in retrospect inaccurate, and the reality of Malawi's experience is that the wide range of malaria control practices in place, including fever management by caretakers and practitioners, constituted a valuable basis for program development. The national program examined interventions, e.g., the effectiveness of CQ in treating children and pregnant women, and then changed policy accordingly. New guidelines were set out for health staff to follow, and plans were implemented. The recommended treatment was then reevaluated, which led to a change in the first-line drug. In effect, Malawi's paradigm for program development was not linear but iterative.

The process of policy and program development is not fixed, not static. The process must be constantly repeated, each step building on what has been learned and done before. Treatment and prevention efforts always need to be evaluated in a systematic manner, and policy and program strategies revised accordingly.

Malawi's experience accrued in the decade before the leadership of WHO and member countries adopted the Global Strategy for Malaria Control in Amsterdam in 1992 (WHO 1993). The Global Strategy defines several control strategies, placing priority on the development of effective malaria case management and prevention services for all populations at risk for malaria infection and illness, both acute uncomplicated and severe. For effective case management, the Global Strategy recognizes that a national program must have data on the current efficacy of antimalarials. Because of changing levels of antimalarial resistance, the strategy emphasizes that guidelines for case management cannot be rigid. The Global Strategy's focus on prevention highlights the importance of malaria prevention in pregnant women and the 'personal protection' potentially provided by insecticide-impregnated bednets. The Global Strategy also emphasizes that a malaria control program capable of providing effective treatment and preventive services will need a monitoring and evaluation mechanism, the results of which may prompt revision of malaria control plans and strategies. Finally, the global strategy acknowledges that for many countries limitations of resources and infrastructure will mean that locally relevant and affordable priorities will need to be established for malaria control.

The internal and international collaboration embraced by Malawi as it forged its National Malaria Control Program influenced the development of the Global Strategy and showed Malawi's position in the context of country-level programs. As noted in Box 9, the information generated from studies in Malawi that evaluated therapy efficacy and prevention effectiveness and set standards for assessing household practices and household and national expenditures has relevance both within the region and globally.

Malawi's experience with malaria control comes at a time when the Global Strategy must define its relevance to local conditions. The translation of Global Strategy to national and local programs is not dictated by formulas, but rather evolves from an assessment of malaria control priorities and of both financial and personnel resources available to the program. The iterative process of monitoring and

evaluation (including operational research) that supports an official planning process embracing prompt and appropriate revisions in malaria control strategies is the core of program operations

The interaction between the Global Strategy and national malaria control programs must be dynamic. Local translation and adaptation of the guidance of the Global Strategy requires national initiative and perspective. In this context, the experience in Malawi has particular value. The national commitment to developing malaria control capacity will continue to evolve concurrently with the renewed global commitment to strengthen malaria control.

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## REFERENCES

**Many of the study results cited in the text have not been published, the study reports reside in the archives of Malawi's Ministry of Health. The following list of references includes published articles cited in this text, reports to the Ministry of Health, and other articles describing research conducted in Malawi during the years 1984-1993**

Barry, M and Molyneux, M 1992 Ethical dilemmas in malaria drug and vaccine trials a bioethical perspective J Med Ethics 18 189-92

Bloland, P B , Kazembe, P , Ziba, C 1991a Chloroquine/fansidar efficacy study, Mangochi, Malawi Report to the Malawi Ministry of Health

Bloland, P B , Redd, S C , Kazembe, P , Tembenu, R , Wirima, J J , Campbell, C C 1991b Co-trimoxazole for childhood febrile illness in malaria-endemic regions Lancet 337 518-20

Bloland, P B , Lackritz, E M , Kazembe, P N , Were, J B , Steketee, R , Campbell, C C 1993 Beyond chloroquine implications of drug resistance for evaluating malaria therapy efficacy and treatment policy in Africa J Infect Dis 167 932-7

Bruce-Chwatt, L J , editor 1986 Chemotherapy of Malaria Geneva World Health Organization

Burnham, G , Harnies, A , Macheso, A , Wirima, J , Molyneux, M 1989 Chloroquine-induced pruritus in Malawi lack of association with onchocerciasis Trans R Soc Trop Med Hyg 83 527-8

Chin, W 1989 Malaria control in Malawi Vector Biology and Control Project AR-121-4

Chitsulo, L , Ettling, M , Macheso, A , Steketee, R , Schultz, L , Ziwa, L 1993 Malaria in Malawi Knowledge, attitudes, and practices Vector Biology and Control Project Report No 82240

Ettling, M , Chitsulo, L, McFarland, D 1993 Malawi The economic impact of malaria on low-income households Vector Biology and Control Project Report No 82239

Ettling, M , McFarland, D A , Schultz, L J , Chitsulo, L 1994a Economic impact of malaria in Malawian households Trop Med Parasitol 45 Suppl 1 74-9

Ettling, M Steketee, R W , Macheso, A , Schultz L J Nyasulu Y Chitsulo L 1994b Malaria knowledge, attitudes and practices in Malawi Survey population characteristics Trop Med Parasitol 45 Suppl 1 57-60

Fogh, S , Jepsen, S , Mataya, R H 1984 R-III chloroquine-resistant *Plasmodium falciparum* malaria from northern Malawi [letter] Trans R Soc Trop Med Hyg 78 282

## References

---

- Fryatt, R J , Teng, J D , Harnes, A D , Moody, A H , Hall, A P , Forsling, M L 1989 Plasma and urine electrolyte concentrations and vasopressin levels in patients admitted to hospital for falciparum malaria Trop Geogr Med 41 57-60
- Goldring, J D , Molyneux, M E , Taylor, T , Wirima, J , Hommel, M 1992 *Plasmodium falciparum* diversity of isolates from Malawi in their cytoadherence to melanoma cells and monocytes in vitro Br J Haematol 81 413-8
- Grau, G E , Taylor, T E , Molyneux, M E , Wirima, J J , Vassalli, P , Hommel, M , Lambert, P H 1989 Tumor necrosis factor and disease severity in children with falciparum malaria N Engl J Med 320 1586-91
- Harnes, A D , Macheso, A , Reeve, P A , Wirima, J J 1988a Lumbar puncture in Malawian patients with altered consciousness Tropical Doctor 18 50-1
- Harnes, A D , Speare, R , Wirima, J J 1988b Symptoms and responses to chemotherapy in adult Malawians admitted to hospital with *Plasmodium falciparum* malaria Ann Trop Med Parasitol 82 511-2
- Harnes, A D , Speare, R , Wirima, J J 1990 Medical admissions to Kamuzu Central Hospital, Lilongwe, Malawi in 1986 comparison with admissions to Queen Elizabeth Central Hospital, Blantyre in 1973 Trop Geogr Med 42 274-9
- Helitzer-Allen, D L , Kendall, C 1992 Explaining differences between qualitative and quantitative data a study of chemoprophylaxis during pregnancy Health Educ Q 19 41-54
- Helitzer-Allen, D L 1993a Examination of the factors influencing utilization of the antenatal malaria chemoprophylaxis program, Malawi, Central Africa [dissertation] Baltimore (MD) Johns Hopkins University
- Helitzer-Allen, D , McFarland, D A , Wirima, J J , Macheso, A F 1993b Malaria chemoprophylaxis compliance in pregnant women a cost-effectiveness analysis of alternative interventions Soc Sci Med 36(4) 403-7
- Heymann DL 1987a Monitoring and Evaluation of CCCD Project Activities, Malawi Report to the Malawi Ministry of Health
- Heymann, D L , Khoromana, C O , Wirima, J J , Campbell, C C 1987b Comparative efficacy of alternative primary therapies for *Plasmodium falciparum* infections in Malawi Trans R Soc Trop Med Hyg 81 722-4
- Heymann, D L , Steketee, R W , Wirima, J J , McFarland, D A , Khoromana, C O , Campbell, C C 1990 Antenatal chloroquine chemoprophylaxis in Malawi chloroquine resistance, compliance, protective efficacy and cost Trans R Soc Trop Med 84 496-8

- Hill, A V , Allsopp, C E , Kwiatkowski, D , Taylor, T E , Yates, S N , Anstey, N M , Wirima, J J , Brewster, D R , McMichael, A J , Molyneux, M E et al 1992 Extensive genetic diversity in the HLA class II region of Africans, with a focally predominant allele, DRB1\*1304 Proc Natl Acad Sci U S A 89 2277-81
- Khoromana, C O , Campbell, C C , Wirima, J J , Heymann, D L 1986 In vivo efficacy of chloroquine treatment for *Plasmodium falciparum* in Malawian children under five years of age Am J Trop Med Hyg 35 465-71
- Lewallen, S , Taylor, T E , Molyneux, M E , Wills, B A , Courtright, P 1993 Ocular fundus findings in Malawian children with cerebral malaria Ophthalmology 100 857-61
- Macheso, A , Nyasulu, Y , Ziba, C , Nwanyanwu, O C , Steketee, R W , Etting, M , Schultz, L J , Chitsulo, L 1994 Malaria knowledge, attitudes, and practices in Malawi Policy implications for the national malaria control program Trop Med Parasitol 45 Suppl 1 80-1
- Maeno, Y , Steketee, R W , Nagatake, T , Tegoshi, T , Desowitz, R S , Wirima, J J , Aikawa, M 1993 Immunoglobulin complex deposits in *Plasmodium falciparum*-infected placentas from Malawi and Papua New Guinea Am J Trop Med Hyg 49 574-80
- Malawi Ministry of Health policy documents Lilongwe
- Guide for management of malaria, 1985-1986 1985
  - Guidelines for the management of malaria for medical officers, clinical officers, medical assistants and nursing staff 1992
  - National malaria control programme, five year implementation plan, 1985-1989 1985
  - National plan for malaria control, 1990-1994 1991
- Mansor, S M , Taylor, T E , McGrath, C S , Edwards, G , Ward, S A , Wirima, J J , Molyneux, M E 1990 The safety and kinetics of intramuscular quinine in Malawian children with moderately severe falciparum malaria Trans R Soc Trop Med Hyg 84 482-7
- Mansor, S M , Molyneux, M E , Taylor, T E , Ward, S A , Wirima, J J , Edwards, G 1991 Effect of *Plasmodium falciparum* malaria infection on the plasma concentration of alpha 1-acid glycoprotein and the binding of quinine in Malawian children Br J Clin Pharmacol 32 317-21
- McDermott, J M , Heymann, D L , Wirima, J J , Macheso, A P , Wahl, R D , Steketee, R W , Campbell, C C 1988 Efficacy of chemoprophylaxis in preventing *Plasmodium falciparum* parasitaemia and placental infection in pregnant women in Malawi Trans R Soc Trop Med Hyg 82 520-3
- Molyneux, M E 1989a Malaria—clinical features in children J R Soc Med 82 Suppl 17 35-8
- Molyneux, M E , Taylor, T E , Wirima, J J , Borgstein, A 1989b Clinical features and prognostic indicators in paediatric cerebral malaria a study of 131 comatose Malawian children [see comments] Q J Med 71 441-59

## References

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Molyneux, M E , Taylor, T E , Wirima, J J , Harper, G 1989c Effect of rate of infusion of quinine on insulin and glucose responses in Malawian children with falciparum malaria BMJ 299 602-3

Molyneux, M E 1990a Cerebral malaria in children clinical implications of cytoadherence Am J Trop Med Hyg 43 38-41

Molyneux, M E 1990b The clinical features of cerebral malaria in children Med Trop 50 65-8

Molyneux, M E , Taylor, T E , Thomas, C G , Mansor, S , Wirima, J J 1991a Efficacy of quinine for falciparum malaria according to previous chloroquine exposure Lancet 337 1379-80

Molyneux, M E , Taylor, T E , Wirima, J J , Grau, G E 1991b Tumour necrosis factor, interleukin-6, and malaria [letter, comment] Lancet 337 1098

Molyneux, M E , Engelmann, H , Taylor, T E , Wirima, J J , Aderka, D , Wallach, D , Grau, G E 1993 Circulating plasma receptors for tumour necrosis factor in Malawian children with severe falciparum malaria Cytokine 5 604-9

Nguyen-Dinh, P , Steketee, R W , Greenberg, A E , Wirima, J J , Mulenda, O , Williams, S B 1988 Rapid spontaneous postpartum clearance of *Plasmodium falciparum* parasitaemia in African women [letter] Lancet 2 751-2

Okitolonda W , Delacollette C , Malengreau M , Henquin J C 1987 High incidence of hypoglycemia in African patients treated with intravenous quinine for severe malaria BJM 295 716-8

Overbosch, D , van den Wall Bake, A W , Stuver, P C , van der Kaay, H J 1984 Chloroquine-resistant falciparum malaria from Malawi Trop Geogr Med 36 71-2

Pappiaoanou, M , Macheso, A , Khoromana, C O , Campbell, C C , Wirima, J J , Heymann, D L 1988 Monitoring clinical response of Malawian children under five years of age with *P falciparum* malaria to treatment with chloroquine during in vivo parasitologic testing Report to the Malawi Ministry of Health

Redd, S C , Bloland, P B , Kazembe, P , Patrick, E , Tembenu, R , Campbell, C C 1992 Usefulness of clinical case-definitions in guiding therapy for African children with malaria or pneumonia Lancet 340 1140-3

Schultz L J , Ettlign, M , Chitsulo, L , Steketee, R W , Nyasulu, Y , Macheso, A , Nwanyanwu, O C 1994a A nation-wide malaria knowledge, attitudes, and practices survey in Malawi Objectives and methodology Trop Med Parasitol 45 Suppl 1 54-6

Schultz, L J , Steketee, R W , Chitsulo, L , Macheso, A , Nyasulu, Y , Ettlign, M 1994b Malaria and childbearing women in Malawi Knowledge, attitudes, and practices Trop Med Parasitol 45 Suppl 1 65-9

- Schultz, L J , Steketee, R W , Chitsulo, L , Wirima, J J 1994c Antimalarials during pregnancy a cost-effectiveness analysis Bull World Health Organ In press
- Schultz, L J , Steketee, R W , Macheso, A , Kazembe, P , Chitsulo, L , Wirima, J J 1994d Efficacy of sulfadoxine-pyrimethamine and chloroquine in preventing peripheral and placental malaria parasitemia in pregnant women J Trop Med Hyg 5 515-22
- Slutsker, L M , Khoromana, C O , Payne, D , Allen, C R , Wirima, J J , Heymann D L , Patchen, L Steketee, R W 1990 Mefloquine therapy for *Plasmodium falciparum* malaria in children under 5 years of age in Malawi in vivo/in vitro efficacy and correlation of drug concentration with parasitological outcome Bull World Health Organ 68 53-9
- Slutsker, L , Taylor, T E , Wirima, J J , Steketee, R W 1993 In-hospital morbidity and mortality due to malaria-associated severe anemia in two areas of Malawi with different patterns of malaria infection Trans Roy Soc Trop Med Hyg In press
- Slutsker, L , Chitsulo, L , Macheso, A , Steketee, R W 1994 Treatment of malaria fever episodes among children in Malawi results of a KAP survey Trop Med Parasitol 45 Suppl 1 61-4
- Steketee, R W , editor 1994 A Nation-wide Malaria Knowledge, Attitudes and Practices Survey in Malawi Trop Med Parasitol 45 Suppl 1 51-82 (Individual articles listed separately)
- Steketee, R W , Divine, B T , Breman, J G , Foster, S O , Campbell, C C 1993a Controlling Malaria in Africa Progress and Priorities ACSI-CCCD ARTS document 099-4051 Atlanta CDC
- Steketee, R W , Taylor T E , Divine, B T , Breman, J G , Campbell, C C 1993b Addressing the Challenges of Malaria Control in Africa ACSI-CCCD ARTS document 099-4072 Atlanta CDC
- Steketee, R W , Wirima, J J , Bloland, P B , Chelima, B , Mermin, J , Chitsulo, L 1993c HIV-1 infection impairs a pregnant woman's acquired ability to limit *Plasmodium falciparum* infection Report to the Ministry of Health
- Steketee, R W , Wirima, J J , Slutsker, L , McDermott, J , Hightower, A W , Bloland, P B , Redd, S C , Breman, J G 1993d Malaria prevention in pregnancy the effects of treatment and chemoprophylaxis on placental malaria infection, low birth weight, and fetal, infant, and child survival ACSI-CCCD ARTS document 099-4048 Atlanta CDC
- Taylor, T E , Molyneux, M E 1988a Cerebral malaria in children presenting features and prognosis Medical Quarterly (Malawi) 5 3-11
- Taylor, T E , Molyneux, M E , Wirima, J J , Fletcher, K A Morris, K 1988b Blood glucose levels in Malawian children before and during the administration of intravenous quinine for severe falciparum malaria [published erratum appears in N Engl J Med 1989 Mar 9, 320(10) 676] N Engl J Med 319 1040-7

## References

---

- Taylor, T E , Molyneux, M E , Wirima, J J , Borgstein, A , Goldring, J D , Hommel, M 1992 Intravenous immunoglobulin in the treatment of paediatric cerebral malaria *Clin Exp Immunol* 90 357-62
- Taylor, T E , Borgstein, A , Molyneux, M E 1993a Acid-base status in paediatric *Plasmodium falciparum* malaria *Q J Med* 86 99-109
- Taylor, T E and Molyneux, M E 1993b Folate deficiency to protect against malaria [letter, comment] *N Engl J Med* 328 1127-8
- Taylor, T E , Wills, B A , Kazembe, P , Chisale, M , Wirima, J J , Ratsma, E Y , Molyneux, M E 1993c Rapid coma resolution with artemether in Malawian children with cerebral malaria [see comments] *Lancet* 341 661-2
- Taylor, T E , Wills, B A , Wirima, J J , Molyneux, M E 1993d Artemether in cerebral malaria [letter] *Lancet* 341 1604
- Teasdale, G , Bennet B 1974 Assessment of coma and impaired consciousness A practical scale *Lancet* 2 81-4
- Vadas, P , Taylor, T E , Chimsuku, L , Goldring, D , Stefanski, E , Pruzanski, W , Molyneux, M E 1993 Increased serum phospholipase A2 activity in Malawian children with falciparum malaria *Am J Trop Med Hyg* 49 455-9
- Warhurst, D C , Hall, A P , Tjokrosonto, S 1985 RI quinine-Fansidar resistant falciparum malaria from Malawi [letter] *Lancet* 2 330
- White N J , Looareesuwan S , Warrell D A , Warrell, M J Chanthavanich, P , Bunnag, D Harinasuta, T 1983 Quinine loading dose in cerebral malaria *Am J Trop Med Hyg* 32 1-5
- White N J , Miller K D , Marsh K , Berry, C D , Turner, R C , Williamson, D H , Brown, J 1987 Hypoglycemia in African children with severe malaria *Lancet* 1 708-11
- Wirima, J J and Harnies, A D 1987 Absence of fever in non-immune patients developing falciparum malaria *British Medical Journal - Clinical Research* 295 913
- Wirima, J , Khoromana, C , Molyneux, M E , Gilles, H M 1988 Clinical trials with halofantrine hydrochloride in Malawi *Lancet* 2 250-2
- Wirima, J J , Khormana, C O , Macheso, A F , Heymann, D L , Campbell, C C 1990 In vivo efficacy of quinine treatment for *Plasmodium falciparum* malaria in Malawian children *Ann Trop Med Parasitol* 84 223-7
- Wirima, J J , Molyneux, M E , Taylor, T E 1991 Cerebral malaria in children (II) causes and treatment of hypoglycaemia before and during treatment *Malawi Medical Journal* 7 9-12



- Wirima, J J 1994 A nation-wide malaria knowledge, attitudes, and practices survey in Malawi Introduction *Trop Med Parasitol* 45 Suppl 1 52-3
- Wolfe, M S , Breman, J G , Ainsworth, B , Teklehaimanot, A , Patchen, L C 1985 Chloroquine-resistant *falciparum* malaria in northern Malawi *Am J Trop Med Hyg* 34 847-9
- World Health Organization 1973 Chemotherapy of Malaria and Resistance to Antimalarials Technical Report Series No 529 Geneva
- World Health Organization 1990 Severe and complicated malaria *Trans R Soc Trop Med Hyg* 84 Suppl 2 1-65
- World Health Organization 1993 Implementation of the global malaria control strategy Technical Report Series No 839 Geneva
- Yamada, M , Steketee, R , Abramowsky, C , Kida, M , Wirima, J , Heymann, D , Rabbege, J , Breman, J , Aikawa, M 1989 *Plasmodium falciparum* associated placental pathology a light and electron microscopic and immunohistologic study *Am J Trop Med Hyg* 41 161-8
- Ziba, C , Slutsker, L , Chitsulo, L , Steketee, R W 1994 Use of malaria prevention measures in Malawian households *Trop Med Parasitol* 45 Suppl 1 70-3