
# The Costs, Effects and Cost-Effectiveness of Changing the First Line Drug for the Treatment of Malaria in Tanzania

**Salim Abdulla[1], Catherine Goodman[2,3], Paul Coleman[2], Godfrey Mubyazi[4], Nassor Kikumbih[1,4] & Tuoyo Okorosobo[5]**

**HEFP working paper 01/00**

[1]Ifakara Health Research and Development Centre (IHRDC), Tanzania

[2]Malaria Consortium of the London School of Hygiene and Tropical Medicine (LSHTM) and the Liverpool School of Tropical Medicine (LSTM)

[3]Health Economics and Financing Programme, London School of Hygiene and Tropical Medicine

[4]National Institute for Medical Research (NIMR), Tanzania

[5]World Health Organisation, Regional Office for Africa (WHO/AFRO)

**ACKNOWLEDGEMENTS**

We are grateful for comments on earlier drafts from Sylvia Meek (Malaria Consortium) and Anne Mills (LSHTM). We would also like to thank the following people for their advice and support: the staff of the Planning & Policy Unit and the National Malaria Control Programme of the Ministry of Health, the Pharmacy Board, Mlimba Health Centre, Kilombero District Health Management Team, the Ifakara Health Research and Development Centre (IHRDC), Tanzanian Essential Health Interventions Project (TEHIP), Adult Morbidity and Mortality Project (AMMP), Medical Stores Department (MSD), Muhimbili Medical Centre, WHO Tanzania Office, WHO Regional Office for Africa, Centres for Disease Control and Prevention, Atlanta (CDC), and UK Department for International Development – Eastern Africa.

Funding for this project was provided by WHO Regional Office for Africa, through the Ministry of Health, Tanzania. Salim Abdulla is supported by the Swiss Agency for Development and Cooperation. Catherine Goodman is a member of the LSHTM Health Economics and Financing Programme, which receives support from the UK Department for International Development

## EXECUTIVE SUMMARY

For decades chloroquine (CQ) has been the official first line drug for the treatment of uncomplicated malaria in nearly all African countries as it is cheap, effective and safe. CQ resistance spread slowly at first, but from the mid-1980s the rate of growth accelerated rapidly; it is now common in practically all endemic countries in sub-Saharan Africa, and Tanzania is no exception. There has been considerable debate in Africa over when the first line drug should be changed, and the choice of replacement drug. It has been proposed that Tanzania change malaria treatment policy from a CQ regimen, with CQ as the first line drug, sulfadoxine-pyramethamine (SP) as second line drug, and quinine as third line drug, to an SP Regimen, with SP as first line, amodiaquine as second line, and quinine remaining as the third line therapy. However, policy makers currently lack information on the impact of the change on health outcomes, the cost implications, and whether the change represents good value for money. As a result this study was commissioned by the National Malaria Control Programme (NMCP) to look at costs, effects and cost-effectiveness of the proposed change in malaria case management

The available information on the effects of the alternative first line drugs is in terms of current parasitological and clinical failure rates only. A decision tree model was therefore used to predict the impact on health outcomes relevant for policy. Estimates for the model input variables were drawn from a review of published and unpublished literature from Tanzania and other African countries, and consultation with researchers and clinicians. The outcomes were estimated for the potential year of switch (year 2000), and the following 9 years with each regimen. Sensitivity analysis was conducted to assess the impact on the conclusions of varying key model input variables.

At current levels of drug resistance, health outcomes in terms of operational treatment failures, number of severe cases and deaths would be significantly better with SP as the first line drug. This is because data from sentinel sites show that drug efficacy is much higher with SP, compliance is expected to be higher, and treatment failure often results in the development of severe disease. Allowing for the growth of drug resistance over time, and making a rough assumption that resistance would grow twice as fast to SP than to CQ as first line drugs, health outcomes would be significantly better on average using SP as first line over the next 5 years, and over the next 10 years. This conclusion is robust to changes in most parameters over reasonable ranges, although given the high levels of uncertainty involved, one cannot completely rule out the possibility that health outcomes would be better with CQ.

Cost information is central to the decision making process to assess the feasibility of the change, plan for its finance, and as an input into the cost-effectiveness evaluation. The impact of the change in policy on the cost of first line drugs to the Ministry of Health (MOH) depends on the number of treatments provided and the average cost per treatment. The number of first line treatments was estimated at 7,7mn per year from Tanzanian Health Information System (MTUHA) data, although there is considerable uncertainty over this figure. The average cost per treatment is a function of both the choice of drug and the mix of formulations used. The cost per treatment is similar for CQ and SP tablets, and a reduction in the use of a syrup formulation could lead to substantial savings in the costs of oral therapy. However it is unclear what drug would be used for cases previously treated with CQ injections, as SP injectables are not available. Assuming that quinine would be used for patients unable to take oral therapy, it was estimated that the net effect of the change in policy would be to increase the costs of providing first line treatment by Tsh 376mn ($482,000) per year.

Reducing treatment failures with the first line drug could lead to significant savings in second and third line drugs, and inpatient care for treatment failures. Baseline estimates indicate that in the first year of the new regimen, cost-savings could recoup over 80% of the incremental cost of the new regimen. Reductions in caseload could also lead to benefits in terms of improved quality of care and reduced costs to patients. Over time the potential for cost-savings would be reduced as the difference between the efficacy of the two alternatives decreased (assuming resistance will grow faster to SP than to CQ as first line drugs).

The process of implementing the policy change is a major task, requiring substantial funding, human resources, expertise, political will, and considerable time. The activities involved include consultation, consensus building and policy formulation, revision and production of treatment guidelines, training of public and private sector health workers, and communication and publicity, and are estimated to cost around Tsh 331mn ($424,000) over an 18 month period. To put this in context, the total cost would be equivalent to around 3% of the MOH annual drugs budget, or 1% of the total annual MOH budget (excluding the change in the costs of drugs).

The results of the analysis of the health impact and costs of the 2 regimens and the costs of implementation were combined to estimate the cost-effectiveness of the policy change. Considering changes in outpatient drug costs only, using the SP regimen rather than the CQ regimen over the 10 year period would cost Tsh 362 ($0.46) per operational failure averted, or Tsh 26,000 ($33) per death averted. If other cost-savings are included the switch appears even more cost-effective. Considering

all drug and non-drug cost-savings the cost per operational failure averted would be Tsh 152 ($0.20), and the cost per death averted Tsh 11,000 ($14). Using the baseline assumptions, the change in policy to the SP regimen appears a highly cost-effective way to improve health outcomes. However, the results should be interpreted with caution, given the high degree of uncertainty involved. Moreover, if the switch led to a substantial increase in SP resistance it could have an adverse impact on future treatment strategies (such as combination therapy), which has not been incorporated in this analysis.

The analysis highlighted several key gaps in information available for drug policy, including treatment failure rates for patients over 5 years, treatment seeking behaviour, the number of antimalarial treatments currently provided and the mix of formulations used, the most efficient way to treat patients who cannot take oral medication if SP becomes the first line drug, the probability of developing severe malaria with early and late treatment failure, and the process of policy change.

**TABLE OF CONTENTS**

**TABLE OF FIGURES**



**TABLE OF TABLES**

## ABBREVIATIONS

| | |
|---|---|
| ACR | Adequate clinical response rate |
| AQ | Amodiaquine |
| CEA | Cost-effectiveness analysis |
| CFR | Case fatality rates |
| CQ | Chloroquine |
| DANIDA | Danish International Development Agency |
| EDP | Essential Drug Programme |
| ETF | Early treatment failure |
| HMIS | Health Management Information System |
| IEC | Information, education and communication |
| IHRDC | Ifakara Health Research and Development Centre |
| IP | Inpatient |
| LSHTM | London School of Hygiene and Tropical Medicine |
| LSTM | Liverpool School of Tropical Medicine |
| LTF | Late treatment failure |
| MOH | Ministry of Health |
| MSD | Medical Stores Department |
| MTUHA | Tanzanian Health Management Information System |
| NIMR | National Institute for Medical Research |
| NMCP | National Malaria Control Programme |
| OP | Outpatient |
| PHC | Primary health care |
| QN | Quinine |
| SMP | Sulfamethopyrazine-pyrimethamine |
| SP | Sulfadoxine-pyrimethamine |
| TEHIP | Tanzania Essential Health Interventions Project |
| TOT | Training of trainers |
| Tsh | Tanzanian Shillings |
| TTF | Total treatment failure |
| WHO | World Health Organization |

# Introduction

## 1.1 Background to malaria treatment policy in Tanzania

Malaria is a leading cause of the burden of disease in Tanzania. A third of all outpatient visits and inpatient admissions, and a quarter of inpatient deaths are attributed to malaria[1], which is also an important cause of chronic anaemia in children and pregnant women, neurological impairment, and low birth weight, and increases the severity of other diseases. The official first line treatment for uncomplicated malaria is chloroquine (CQ), which is the only antimalarial available in most health centres and dispensaries. Second and third line therapies (sulfadoxine-pyrimethamine (SP) or sulfamethopyrazine-pyrimethamine (SMP), and quinine) are available at hospitals[2].

For decades CQ has been the official first line drug for the treatment of uncomplicated malaria in nearly all African countries as it is cheap, effective and safe. CQ resistance spread slowly at first, but from the mid-1980s the rate of growth accelerated rapidly; it is now common in practically all endemic countries in sub-Saharan Africa, and Tanzania is no exception. Recent sentinel site surveys found treatment failure in between 28% and 72% of patients[3]. There has been considerable debate in Africa over when the first line drug should be changed, and the choice of replacement drug[4]. A common candidate is SP, which currently faces treatment failure rates in Tanzania of 6% to 34%[3]. A change to SP has already been implemented in a few African countries (Malawi, Kenya, Botswana and South Africa), but most continue to use CQ, despite high levels of resistance and reports that resistance is associated with a rise in malaria related mortality[5].

It has been proposed that Tanzania change malaria treatment policy from a CQ regimen, with CQ as the first line drug, SP as second line drug, and quinine as third line drug, to an SP regimen, with SP as first line, amodiaquine as second line, and quinine remaining as the third line therapy[3]. A key question for policy makers in Tanzania is whether such a change should be implemented, and if so when. Reluctance to change policy stems from several factors including poor information on current levels of resistance and their health impact, and concern about the cost implications. In addition, the potential growth of resistance to SP is a major cause of concern for policy makers, who fear that this drug will soon also require replacement, and are aware that few other safe, effective and affordable antimalarials are available. Whereas SP and CQ are relatively similar in price per treatment, the potential replacements for SP are much more expensive. In some areas of South East Asia SP has been replaced with mefloquine, which has a cost per treatment 30 to 40 times greater than CQ, and is

unlikely to be affordable in sub-Saharan Africa.

## 1.2 Rationale for Study

The factors affecting the decision to change are numerous and complex, covering epidemiological, economic, behavioural, and safety issues, and involving consideration of both current outcomes and future trends. Policy makers currently lack information on the impact of a change in policy on health outcomes, the cost implications, and whether the change represents good value for money. Discussions with the technical committee of the National Malaria Control Programme (NMCP) led to the identification of the following key data requirements for informing policy change: drug efficacy, health seeking behaviour, cost and cost-effectiveness. As a result, an "Assessment of the Efficacy and Cost-effectiveness of the Antimalarial Treatments in Tanzania" was commissioned by the NMCP. Component 1 covered the collection of primary data on antimalarial efficacy and effectiveness, Component 2 the collection of household and provider costs, and Component 3 utilised these data to explore the costs, effects and cost-effectiveness of the proposed change in first line drug. The results of Component 3 are reported here. Component 3 was undertaken as a collaboration between researchers from the Ifakara Health Research and Development Centre, the National Institute for Medical Research and the Malaria Consortium of the London School of Hygiene and Tropical Medicine (LSHTM) and the Liverpool School of Tropical Medicine (LSTM), drawing on staff members from the LSHTM Health Economics and Financing Programme. Financial support was provided by the WHO Regional Office for Africa.

## 1.3 Outline of report

The study considered the health impact and costs over the next decade of both remaining with the CQ regimen and changing to the SP regimen. In Chapter 2 a decision tree model is used to assess the impact on health outcomes. Chapter 3 considers the cost implications, and potential cost-savings from the change, and in Chapter 4 the process of implementing the policy change is discussed and budgeted. Chapter 5 synthesises the results reported in chapters 2, 3 and 4 in order to estimate the cost-effectiveness of the proposed change in policy. Finally Chapter 6 highlights key conclusions and priorities for future data collection.

# 2 The Impact on Health Outcomes

## 2.1 Introduction

The aim of this chapter is to quantify the potential health effects of the proposed change in treatment policy from the CQ regimen to the SP regimen. The available information on the effects of the alternative first line drugs is in terms of their current parasitological and clinical treatment failure rates, standardised measures of the proportion of treated cases which do not resolve or are subject to recrudescence under supervised conditions. These efficacy measures are inadequate for policy making for several reasons. Firstly they are made under very controlled conditions, where the intake of drugs is carefully monitored, and do not capture the effectiveness of the drugs under operational conditions where non-compliance may be common. Secondly policy makers need information not only on cure rates, but also on the impact of drug resistance on health facility utilization (e.g. inpatient admissions) and final health outcomes (e.g. mortality). Finally, only current estimates are available, but policy makers need to know how drug efficacy, facility utilization and final health outcomes are likely to change over time as resistance grows. A model was therefore used to predict the impact on outcomes relevant for policy.

## 2.2 Methods

The model used estimates of compliance, treatment seeking behaviour, the probability of developing severe disease, and case fatality rates to extrapolate from the available drug efficacy data to health and utilization outcomes. The analysis was based on a decision tree model of patients with suspected uncomplicated malaria presenting at an outpatient facility in sub-Saharan Africa[6, 7], which was adapted to the Tanzanian context. The decision tree traces the possible paths a presenting patient could follow, with probabilities attached to each option or branch of the tree. For example, for a patient with treatment failure, probabilities are assigned to reflect the likelihood of remaining with uncomplicated malaria or developing severe disease. If the latter, probabilities are estimated for the likelihood of seeking admission to hospital, and the case fatality rate with and without inpatient treatment.

For a given probability of total treatment failure (TTF) (defined as clinical failure and parasitaemia by day 14 following treatment[8]), the model provides estimates of the probability of the following outcomes:

- operational failure following the first outpatient visit (which is a function of both TTF and non-compliance)
- developing severe malaria during this episode
- inpatient admission during this episode
- death as a result of this episode.

These outcomes can be estimated both for all patients with suspected uncomplicated malaria on the basis of clinical diagnosis, and for the sub-set of these patients with true malaria (estimated at 46% of those clinically diagnosed – see Annex 1). The health effects in this chapter are presented just for patients with true malaria, as the outcomes for false positive cases would not be affected by a change in the antimalarial used. (However, as all patients with suspected malaria would be treated, the cost and cost-effectiveness estimates in chapters 3 and 5 are calculated for all patients.)

Estimates for the model input variables were drawn from a review of published and unpublished literature from Tanzania and other African countries, and consultation with researchers and clinicians. As data are very patchy for many of these variables, the model inevitably involves the use of several estimates and assumptions, and all model conclusions should therefore be regarded as tentative. The mortality estimates are particularly uncertain, as the case fatality rate for severe patients not receiving inpatient care is unknown.

The clinical failure rates in 1999 for children under 5 years were approximated as the mean TTF from recent sentinel site surveys in Tanzania, giving estimates of 50% with CQ, 14% with SP and 5% with amodiaquine. The proposed policy change would affect all age groups, but no data were available on treatment failure rates for patients over 5 years of age, nor were data sets available from other African countries comparing clinical failure in different age groups. In areas of stable malaria endemicity, one would expect lower failure rates in higher age groups, as older patients are more likely to exhibit acquired immunity. A rough estimate was therefore made that TTF in patients over 5 years of age would be half that in patients under 5.

To estimate the health outcomes in future years with either regimen it was necessary to make assumptions about the growth rates of drug resistance over time. The growth rate of resistance to CQ was estimated by fitting a logistic growth function to rough historical estimates made by a group of experts of CQ total treatment failure in children under 5 years over the last 50 years[3]. These historical estimates can only be considered as rough approximations, as they are based on limited data

points, with haphazard geographical coverage and non-comparable methodology. Estimates were made of the likely growth rates of resistance to the other drugs, depending on the characteristics of each drug, such as their half-lives, and their role in the official regimen. It is expected that resistance will grow more quickly to SP than to CQ from a given baseline level if used as a first line drug, because of differences in the mechanisms by which resistance to the two drugs develops, and because SP persists for longer in the patient's blood. However, we do not know how much faster resistance to SP will grow, and it was therefore necessary to make a rough estimate. As a baseline assumption it was assumed that once SP was adopted as the first line drug, the growth rate of resistance would be twice that of the growth rate of CQ resistance. (The relative growth rates of resistance to CQ and SP were varied in the sensitivity analysis to test the significance of this assumption.) Figure 2.1 shows the historical estimates and fitted functions for CQ resistance, assuming it was maintained as first line drug. It also shows the estimated function for SP resistance assuming that it was adopted as first line in 2000 and that SP resistance grow twice as fast as CQ resistance. The fitted functions predict that average CQ TTF in under fives will be 53.1% in the year 2000, and that if the CQ regimen is maintained, CQ TTF will increase to 65% in 2004, and 77% in 2009. The SP TTF for under fives is predicted to be 15% in 2000, and if SP were introduced as first line drug in that year, its TTF is predicted to increase to 32% in 2004, and 61% in 2009. Because current levels of SP resistance are already relatively high, the average year on year increase over the next decade is expected to be very rapid.

The outcomes were estimated for the potential year of switch (year 2000), and the following 9 years with each regimen. The time frame used to compare the regimens should depend on the number of years before it is believed that an alternative feasible therapy will become available, such as a new drug or a combination therapy. As a rough guide the predicted outcomes with each regimen were averaged over the five year period 2000-2004 and the ten year period 2000-2009.

Full details of the model design, calculation methods and input parameters are presented in Annex 1.

## 2.3 Model Results

### 2.3.1 Estimating intermediate health and utilization outcomes

Table 2.1 shows predicted outcomes with both regimens in the year 2000. With CQ as the first line drug, of under fives with malaria treated at outpatients, 66% would experience operational failure with

the first line drug (due to either drug resistance or non-compliance); 18% would develop severe disease at some stage during the episode; and 8% would be admitted as inpatients. For patients over five years, 47% would experience operational failure with the first line drug; 0.8% would develop severe disease; and 0.3% would be admitted as inpatients.

If a change were made to the SP regimen in the year 2000, there would be a fall in the operational failure rate in under fives to 26%, only 6% would develop severe disease, and 3% would be admitted as inpatients. For over fives 19% would experience operational failure, 0.3% would become severe, and 0.1% would be admitted.

The change in regimen would therefore lead to substantial improvements in health outcomes in 2000. Considering all age groups, there would be a reduction in operational failure with the first line treatment of a third, and the probability of developing severe disease would fall from 7.7% to 2.7%. This is mainly because resistance levels are far lower with SP, but also because compliance is expected to be higher with SP as it is a single dose drug, so there is less difference between TTF and operational failure rates. For an estimated annual number of initial outpatient visits for suspected malaria in Tanzania of 9,1mn (see Annex 2), and assuming that 46% of these are true malaria, this would imply a reduction in operational failures of around 1,4mn, a reduction in the number of severe cases of 210,000 and a reduction in inpatient admissions of 89,000.

The estimated growth rates of resistance were used to predict how the outcomes would change over time. For patients under five, Figure 2.2 shows the predicted TTF and operational failure rates, and Figure 2.3 shows the probability of developing severe malaria and inpatient admission following treatment failure with both regimens for 2000 to 2009. If the CQ regimen were maintained, resistance would continue to grow to CQ, leading to an increase in operational failures, severe cases and inpatient admissions. The model predicts that by 2004, 75% of under fives would experience operational failure, 21% would become severe and 9% would be admitted. By 2009, 84% of under fives would experience operational failure, 24% would become severe and 10% would be admitted.

If a change were made to the SP regimen in the year 2000 the model predicts that there would initially be a substantial improvement in all outcomes as described above, which would then deteriorate over time as resistance to SP increased rapidly once it was adopted as first line. By 2004, 40% of under fives would experience operational failure, and by 2009 66%, so by the end of the 10 year period, health outcomes with the SP regimen would be roughly equal to those with the CQ regimen in 2000.

For the five year period 2000-2004 and the 10 year period 2000-2009 Table 2.2 shows the average values of each outcome with each regimen and the ratio between the two regimens. A ratio below one indicates that the health outcomes would be better with the SP regimen. Over the five year period the SP regimen clearly performs better than with the CQ regimen for all outcomes and in both age groups. For example, the average operational failure rate for all ages over the 5 years would be 57.8% with CQ but 26.5% with SP, and the average probability of becoming severe would be 8.3% with CQ and 3.6% with SP. The ratio of the SP regimen to the CQ regimen is between 0.43 and 0.46 in each case, meaning that changing to SP in 2000 leads to a roughly 55% improvement in health outcomes. If a 10 rather than 5 year period is considered, the difference between the two regimens is slightly reduced as it is assumed that the growth of resistance to SP is faster, so the outcomes are closer during 2005-9 than during 2000-4. However, even over 10 years the average outcomes are clearly better with SP than with CQ in both age groups. The ratio of the SP regimen to the CQ regimen is between 0.54 and 0.58, equivalent to an approximate improvement in health outcomes of 45%. This implies an average annual reduction in the number of operational failures over the 10 years of 1,3mn, in the number of severe cases of 200,000, and in the number of inpatients of 84,000.

### 2.3.2 Estimating the impact on mortality

Estimating mortality is highly speculative. In addition to all the assumptions necessary to calculate the other health and utilization outcomes, it also requires the estimation of case fatality rates (CFRs) for patients with severe malaria. Relatively good estimates can be made from MTUHA data for patients who are admitted as inpatients. In 1996 data from hospital inpatient records showed a CFR for inpatients of 2.9% for under fives and 2.4% for over fives[1]. However, there is no information on the CFR of severe cases who do not seek inpatient care. As the assumptions about the CFR affect both regimens equally, they do not alter conclusions about their relative effectiveness, but they do have a substantial impact on the predicted absolute number of deaths averted. Baseline assumptions were made of a CFR for severe cases not admitted of 15% in under fives and 7% in over fives. (This compares with an average estimated by fourteen experienced paediatricians of 14% for Kenyan children under five with severe malaria deprived of inpatient care[9]). These baseline assumptions produced an estimated probability of dying during this episode of malaria with the CQ regimen in 2000 of 1.8% in under fives, 0.04% in over fives, giving a weighted average of 0.7%. Using the SP regimen in the same year implies a probability of dying of 0.6% in under fives, 0.02% in over fives, and a weighted average of 0.3% (Table 2.1). Figure 2.4 shows the probability of death in patients under five years following treatment failure with both regimens for 2000 to 2009. Applying these figures to the

estimated annual number of initial outpatient visits implies a reduction in the number of deaths of around 20,000 in the year 2000. Over the five year period using the SP regimen would avert an average of 19,000 deaths per year, or an average of 16,000 per year over the 10 year period. Reducing the assumed CFR with no inpatient care to 10% in under fives and 5% in over fives reduces the average deaths averted to 14,000 per year over the five year period and 11,000 per year over 10 years. Increasing the CFR with no inpatient care to 30% in under fives and 15% in over fives increases the average deaths averted to 36,000 per year over the five year period and 30,000 per year over 10 years.

## 2.4 Sensitivity Analysis

There is a high degree of uncertainty about many other parameter estimates used in the model. In order to attach probabilities to the decision tree, it was necessary to use some data from specific areas of Tanzania which may not be representative for the whole country, some estimates from other countries, and for some variables there were simply no data available, so it was necessary to rely purely on expert opinion. The impact on the outcomes of changing input variables was explored using sensitivity analysis, where inputs are varied to test the robustness of the conclusions of the analysis. Figure 2.5 shows the results of a one-way sensitivity analysis (inputs varied one by one) for one of the key outputs: the ratio between the SP and CQ regimens of severe cases in all ages, over the 10 year time period (a ratio below one implying better average outcomes with the SP regimen). For the baseline assumptions the ratio was 0.57. The ratio remained under one for changes in many of the input parameters over reasonable ranges, such as reducing the initial CQ TTF, increasing the initial SP TTF, reducing the TTF ratio between over and under fives, increasing CQ compliance, increasing the availability of the second line drug, doubling the growth of resistance to all drugs, or increasing the growth rate of resistance to SP relative to CQ from 2 to 4 times. The model results are most sensitive to the initial levels of drug resistance and the relative growth rates of resistance to SP and CQ. Threshold analysis was conducted to see at what ratio between the resistance growth rates the CQ regimen would become more effective. Holding other input values constant, if resistance to SP grew 6 times as fast as resistance to CQ, the two regimens would be roughly equal in effectiveness, and at any ratio higher than this, the CQ regimen would be preferable.

One-way sensitivity analysis tends to underestimate the true variability in outcomes as only one variable can be changed at a time. Figure 2.6 shows the results of a multi-way analysis, where several of the input variables are changed at once. Whether the SP regimen remained more effective depended on the combination of variables changed. For example, reducing the initial CQ TTF in under

fives to 40% and over fives to 20%, and increasing the growth rate of resistance of SP relative to CQ from 2 to 3, only increased the ratio to 0.81. However, reducing the initial CQ TTF in under fives to 30% and over fives to 15%, and increasing the growth rate of resistance of SP relative to CQ from 2 to 4, increased the ratio to 1.10, making the CQ regimen look more attractive.

It is evident that the results are dependent on the input parameters used, many of which are subject to a high level of uncertainty. The model cannot therefore provide definitive predictions about the impact of using the two regimens. However, it can be used as an analytical tool to help structure the problem, and explicitly explore the impact of varying key input variables on health outcomes. The conclusion that the SP regimen would be more effective on average over the 10 years appears relatively robust to a wide range of variation in parameter inputs. It should be noted that if the 5 year, rather than 10 year period had been used for the sensitivity analysis the results would have been more favourable to SP. In addition, some analysts would argue that a discount rate should be used to place less weight on health benefits that occur further into the future. Incorporating discounting would also make the SP regimen look relatively more attractive, as it would put more weight on earlier years when the differential in favour of SP is greater.

**Figure 2.1** Predicted growth rates of Total Treatment Failure (TTF) in patients under five with CQ or SP regimen: historical estimates and fitted function for CQ TTF (assuming maintained as first line drug) and estimated function for SP TTF (assuming introduced as first line drug in 2000, and that growth rate of resistance to SP is twice growth rate of resistance to CQ).

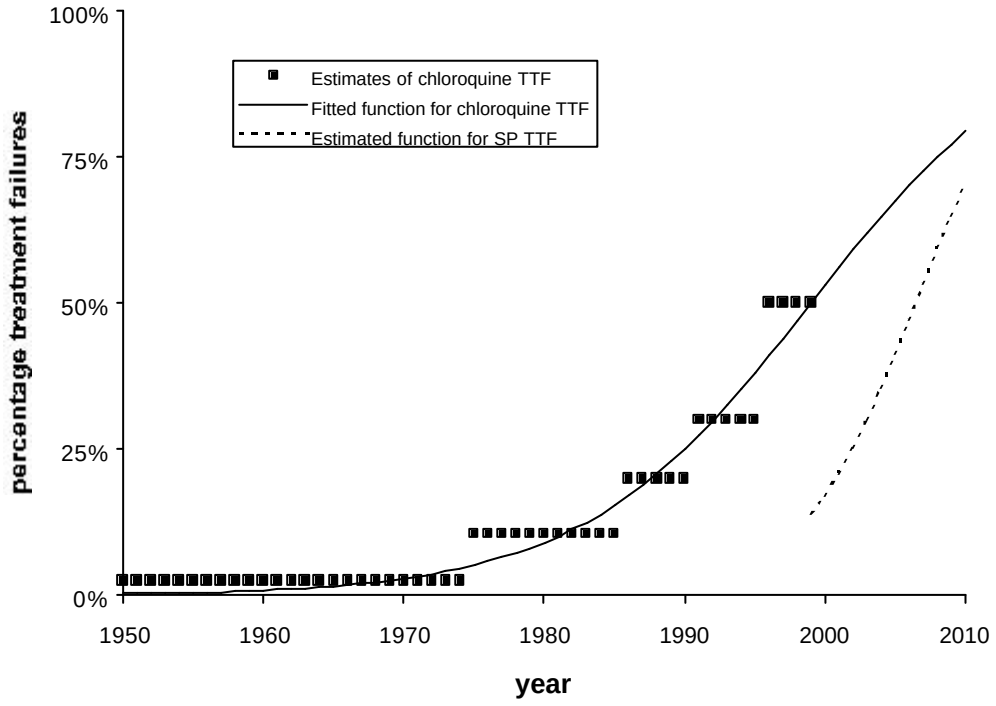


**Figure 2.2** Percentage of out-patients under five with malaria experiencing total treatment failure, and operational failure after first visit with either CQ maintained as first line, or SP introduced as first line in 2000.

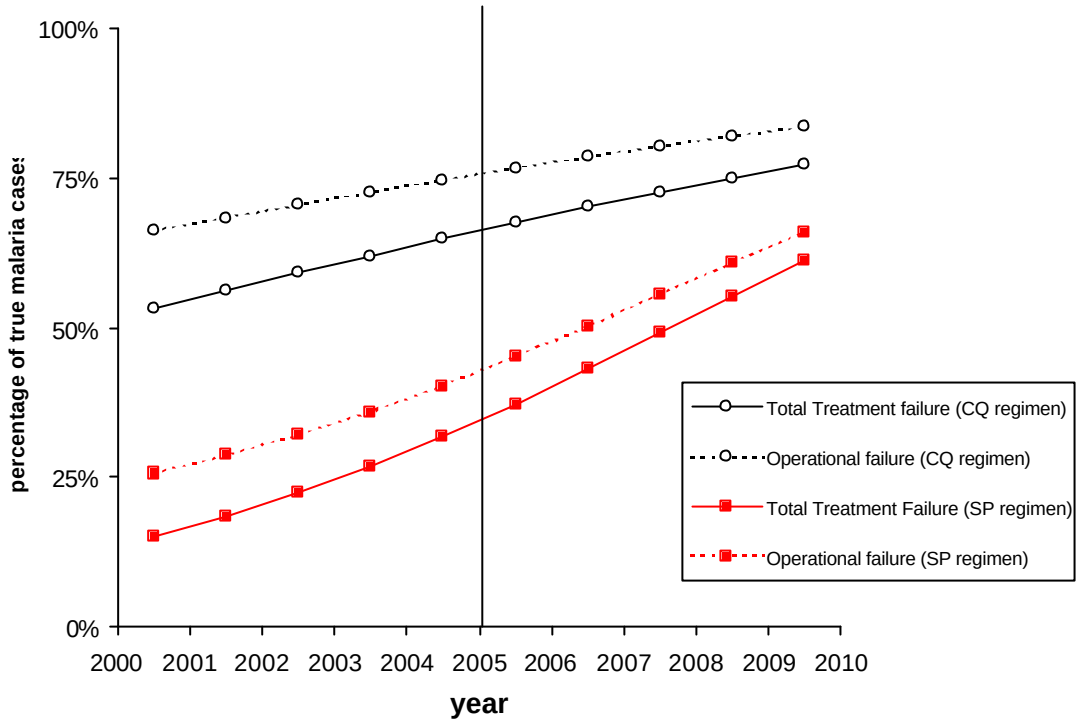



**Figure 2.3** Percentage of out-patients under five with malaria becoming severe, and percentage being admitted as inpatients following treatment failure with either CQ maintained as first line, or SP introduced as first line in 2000.

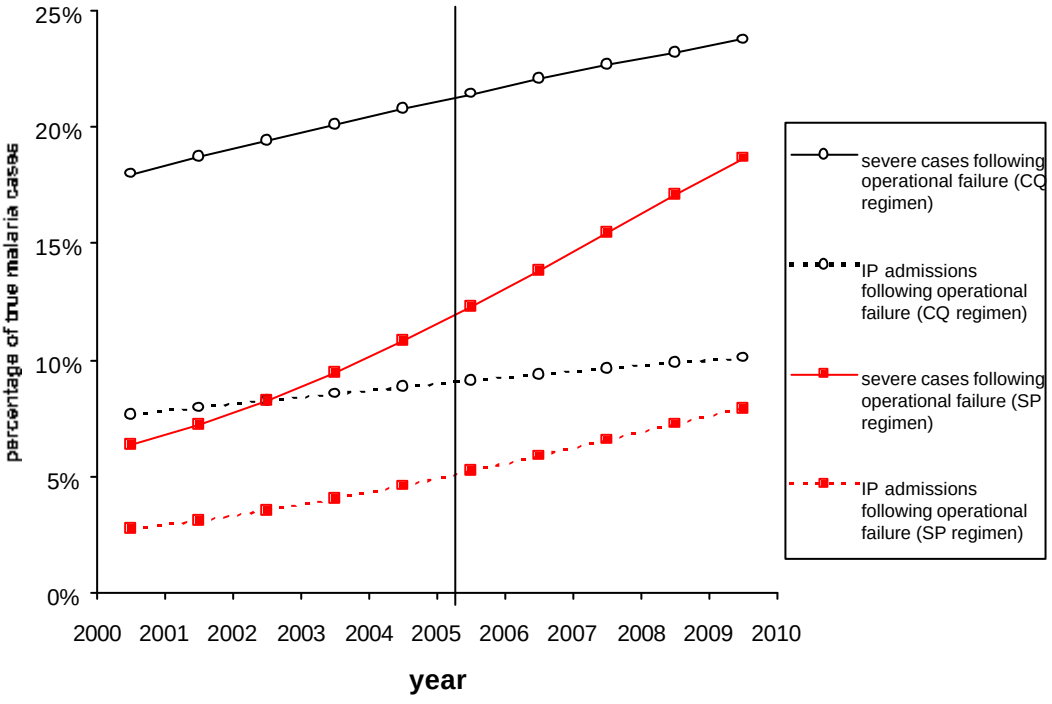


**Figure 2.4** Percentage of out-patients under five with malaria dying following treatment failure with either CQ maintained as first line, or SP introduced as first line in 2000

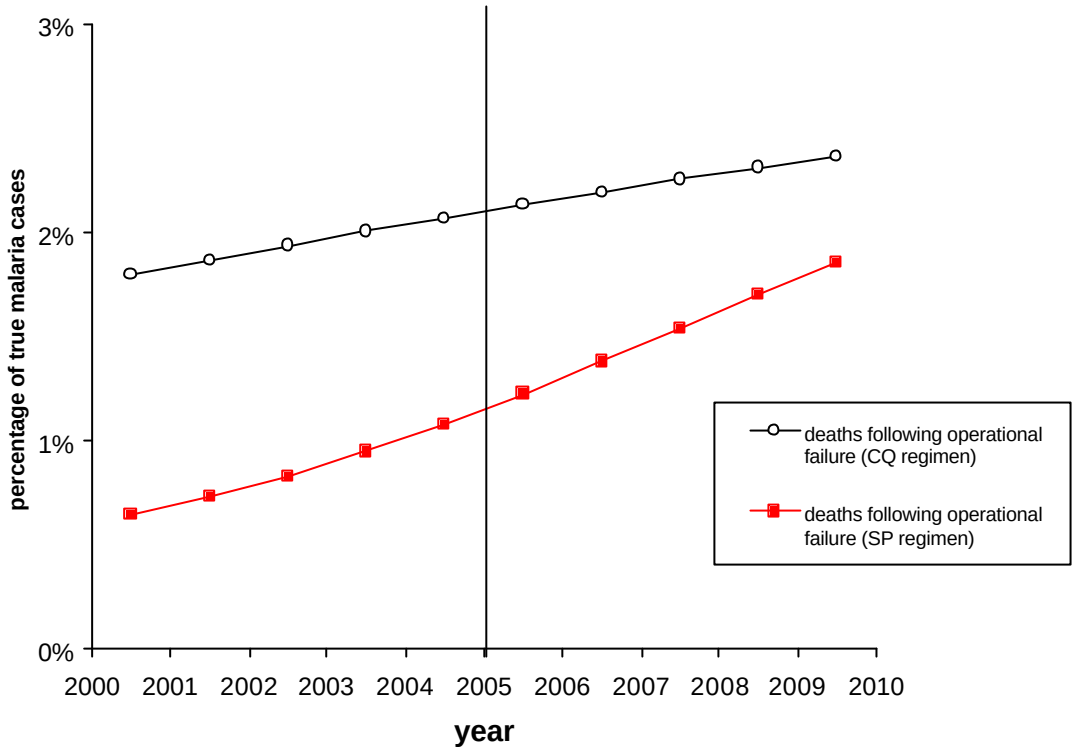


**Figure 2.5** One-way sensitivity analysis of the probability of developing severe malaria (all ages, over the 10 year time period): ratio between SP & CQ regimens.

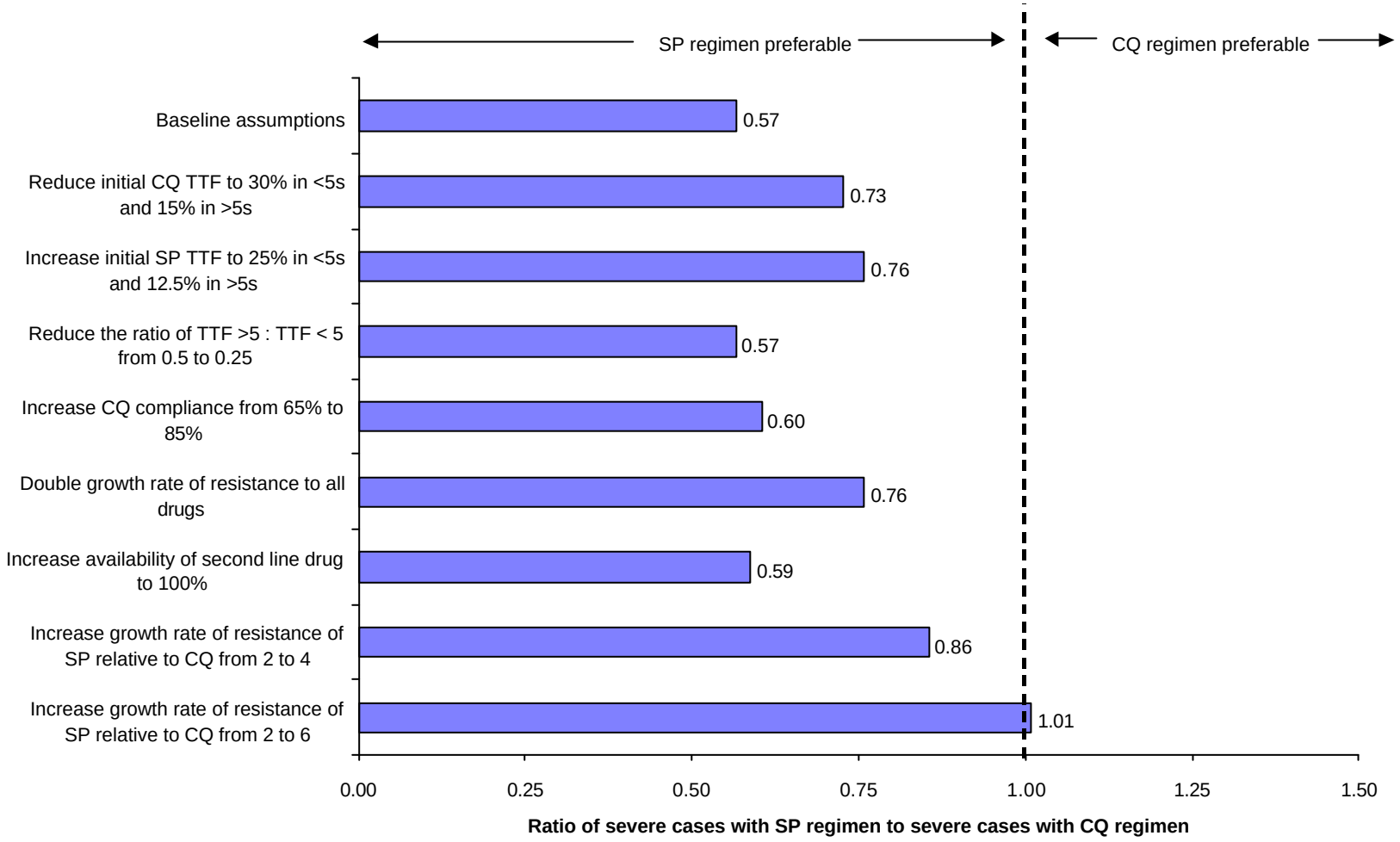
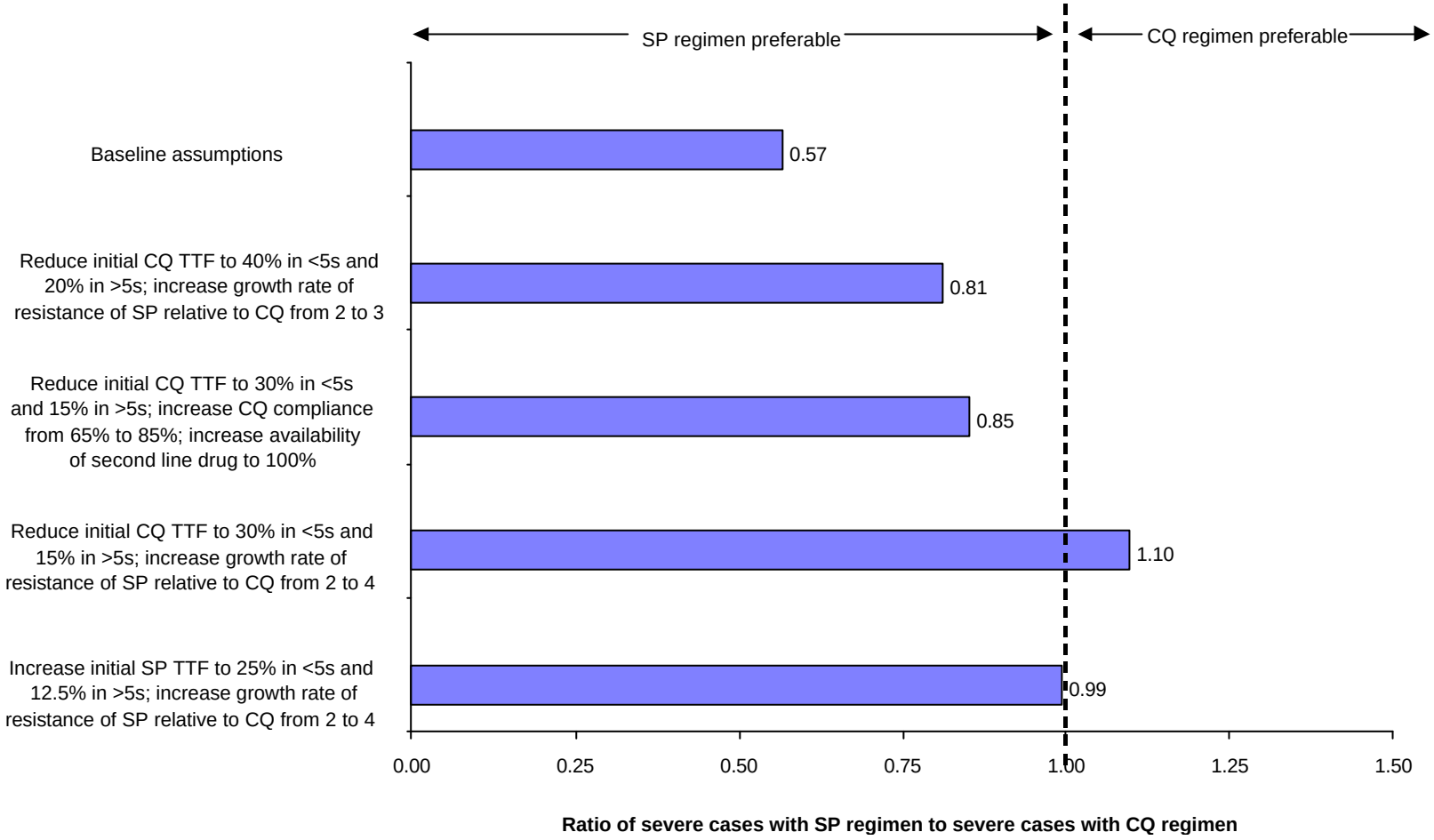


**Figure 2.6** Multi-way sensitivity analysis of the probability of developing severe malaria (all ages, over the 10 year time period): ratio between the SP and CQ




regimens.

**Table 2.1** Estimated outcomes for the year 2000 with either CQ maintained as first line or SP introduced as first line in 2000: patients in each category as percentage of all those presenting with true uncomplicated malaria at an outpatient facility

| | CQ regimen | | | SP regimen | | |
|---|---|---|---|---|---|---|
| | <5 years | >5 years | All ages | <5 years | >5 years | All ages |
| Total Treatment Failure (TTF) | 53.1% | 26.6% | 37.2% | 15.0% | 7.5% | 10.5% |
| Operational failure | 66.2% | 47.1% | 54.8% | 25.6% | 19.1% | 21.7% |
| Develop severe malaria | 18.0% | 0.8% | 7.7% | 6.4% | 0.3% | 2.7% |
| Inpatient admission | 7.7% | 0.3% | 3.3% | 2.7% | 0.1% | 1.2% |
| Death | 1.8% | 0.04% | 0.7% | 0.6% | 0.02% | 0.3% |

**Table 2.2** Average probabilities for health and utilization outcomes over the five year period 2000-2004, and the 10 year period 2000-2009 for each regimen.

**Average probability over 5 year period (2000-2004)**

| | CQ regimen | | | SP regimen | | | Ratio SP regimen : CQ regimen | | |
|---|---|---|---|---|---|---|---|---|---|
| | <5 years | >5 years | All ages | <5 years | >5 years | All ages | <5 years | >5 years | All ages |
| Operational failure | 70.5% | 49.3% | 57.8% | 32.5% | 22.5% | 26.5% | 0.46 | 0.46 | 0.46 |
| Develop severe malaria | 19.4% | 0.9% | 8.3% | 8.4% | 0.4% | 3.6% | 0.43 | 0.43 | 0.43 |
| Inpatient admission | 8.3% | 0.4% | 3.5% | 3.6% | 0.2% | 1.5% | 0.44 | 0.43 | 0.44 |
| Death | 1.9% | 0.05% | 0.8% | 0.8% | 0.02% | 0.4% | 0.44 | 0.43 | 0.44 |

**Average probability over 10 year period (2000-2009)**

| | CQ regimen | | | SP regimen | | | Ratio SP regimen : CQ regimen | | |
|---|---|---|---|---|---|---|---|---|---|
| | <5 years | >5 years | All ages | <5 years | >5 years | All ages | <5 years | >5 years | All ages |
| Operational failure | 75.4% | 51.7% | 61.2% | 44.0% | 28.3% | 34.6% | 0.58 | 0.55 | 0.57 |
| Develop severe malaria | 21.0% | 0.9% | 9.0% | 12.0% | 0.5% | 5.1% | 0.57 | 0.54 | 0.57 |
| Inpatient admission | 8.9% | 0.4% | 3.8% | 5.1% | 0.2% | 2.2% | 0.57 | 0.54 | 0.57 |
| Death | 2.1% | 0.05% | 0.9% | 1.2% | 0.03% | 0.5% | 0.57 | 0.54 | 0.57 |

# 3 The Impact on Costs

## 3.1 Introduction

The cost implications of the change in drug regimen are a key concern for policy makers. Cost information is central to the decision making process to assess the feasibility of the change, plan for its finance, and as an input into the cost-effectiveness evaluation. In addition to the incremental costs of the drugs, policy makers need to know whether there are likely to be significant cost-savings from reducing the need to care for treatment failures when a more effective first line drug is used.

This chapter begins with a brief background to the provision and financing of antimalarials in Tanzania. Estimates are then made of the incremental drug costs for the Ministry of Health (MOH) of changing regimen, by combining information on the number of cases treated and the cost per treatment. Potential cost savings for the MOH are then considered in outpatient drugs, inpatient drugs and other costs of inpatient care to estimate the net cost of the change. Consideration is also given to the likely impact on costs to patients.

## 3.2 The provision and financing of antimalarials in Tanzania

All drugs for public health facilities are procured and distributed through the Medical Stores Department (MSD), which is an autonomous department within the MOH. For the financial year 1999/2000 a total of Tsh 10,9bn was budgeted for drugs and associated medical supplies, Tsh 9,5bn by the Government and Tsh 1,4bn by DANIDA(10)[1]. MSD has estimated that 7% of total public expenditure on drugs and medical supplies is for antimalarials(11).

There are two mechanisms for distributing drugs to health facilities.

a) Health Centres and Dispensaries. These primary health care (PHC) facilities are provided with Essential Drug Programme (EDP) Kits on a monthly basis. 80% are basic yellow kits for Dispensaries, and 20% more comprehensive blue kits for Health Centres. They contain all the drugs to be used by these facilities, and are generally of a standard composition[2]. The only antimalarial in either standard kit is CQ, in tablet, syrup and injectable formulation. In 1999/2000 a total of Tsh 6,4bn was budgeted for the kits. The kits were originally funded by DANIDA, but the

[1] Exchange Rate in August 1999 was Tsh 780 / US$.
[2] There are some variations to this standard system, such as the distribution of an extra "top-up" kit in 1999, the provision of additional drugs for facilities participating in the Integrated Management of Childhood Illness

Government has taken increasing responsibility for covering their costs, and in 1999/2000 was contributing 78% of kit costs. The kit delivery system is highly effective, with a recent audit by Price Waterhouse Coopers reporting that over 97% of kits arrive at the designated facility[12]. In theory the kits should last for the whole month. However in practice there are frequent reports of drug stockouts. Several studies have found that it is common for health facilities to run out of certain drugs by the third or fourth week of the month [13, 14], and in a recent study in Kibaha over 85% of mothers reported a lack of drugs at public health facilities at their last visit[15]. It is not clear what the overall frequency of stockouts is, or to what degree they are caused by genuine shortages, as opposed to leakage or inappropriate prescription.

b) Hospitals. Hospitals can order any drugs on the essential drugs list to be distributed by MSD. The drugs are funded from budgets deposited by the government for each district at MSD. In 1999/2000 Tsh 4,0bn was budgeted for hospital drugs[3]. The antimalarials supplied are CQ (tablets, syrup and injectables), SP (tablets), SMP (tablets), and quinine (tablets and injectables).

## 3.3 Expenditure on the first line therapy

The impact of the change in policy on the cost of first line drugs to the MOH depends on the number of treatments provided and the average cost per treatment.

### 3.3.1 The number of first line treatments provided

Using data from the Tanzanian Health Information System (MTUHA), scaled up to compensate for the reporting rate of only 51%, it was estimated that 10mn outpatient diagnoses of malaria are made each year in Tanzania, and that 9mn of these would be initial visits (i.e. first visits for a given episode) (see Annex 2). Due to the occurrence of stockouts, not all of these patients would receive drugs. Using an estimated stockout rate of 15%, the number of visits where the first line antimalarial is provided would be 7,7mn. Where a stockout was experienced the patient or caretaker may choose to purchase the prescribed drug over the counter. In this situation, the drugs would not represent a cost to the provider, although the costs would be incurred by patients.

It is important to distinguish between:

a. the cost of providing enough SP to replace the initial CQ treatments currently provided,

---

(IMCI), and the piloting of a new "indent" system, whereby PHC facilities can order the specific drugs they require from the essential drugs list.

[3] A further Tsh 0,5bn has been budgeted for other drug items (Emergency, Clearing/Forwarding, and Vertical Programmes)[10]

b. the cost of providing enough SP for all initial outpatient visits, and

c. the cost of providing sufficient SP to meet the true need in community.

The following calculations are designed to estimate (a) only, but due to the frequency of drug stockouts, (b) will be greater than (a), and due to utilization of alternative non-governmental sources of health care, (c) will be greater than (b).

### 3.3.2 The change in the average cost per initial treatment

The average cost per treatment with a range of antimalarial drugs and formulations is shown in Table 3.1 for patients under and over five years. Prices were available from the MSD Essential Drugs and Medical Supplies catalogue[16] for all drugs except Amodiaquine, for which an average price from the International Drug Price Indicator Guide[17] was used. (As drug prices depend on the volume ordered, unit prices might change if there were a significant shift in the ordering pattern of MSD following a change in the official regimen.) An estimated 10% drug wastage overall was included in the price of each treatment. The data for under fives are also shown graphically in Figure 3.1. In tablet form CQ is the cheapest, at an average of Tsh 9 for a child under 5 and Tsh 55 for patients over five. SP tablets are only marginally more expensive, at Tsh 11 for under fives and Tsh 66 for over fives. Amodiaquine tablets are roughly twice the cost of SP at Tsh 23 and Tsh 138, SMP tablets costs Tsh 33 and Tsh 198, and a 7 day oral course of quinine is much more expensive at Tsh 158 and Tsh 947. There is substantial variation in the cost of different formulations of the same drug as well as between drugs. For example, in injection or syrup form the cost of CQ exceeds that of both SP and Amodiaquine tablets. A course of CQ injections for an under 5 costs Tsh 66 and for an over 5, Tsh 204 (including the cost of the syringe), and treatment with CQ syrup, the formulation of preference for the under 5 age group, costs Tsh 52. Moreover, if it is not possible to decant the required syrup dose into a container, it may be necessary to provide a whole bottle of syrup to caretakers, increasing the cost several fold.

Whether the average drug cost per treatment increases or decreases following a change in first line drug is therefore dependent not only on the choice of drug, but also on the balance of formulations provided. SP is not available as a syrup so all those who can take oral medicine are likely to be given tablets, which should significantly reduce the average cost of *oral* therapy for children. It is not clear what the new policy will be for patients who are unable to take oral medication and currently receive CQ injections. An injectable form of SP exists, but is not widely available in Africa. In both Malawi and South Africa where the first line drug has already been changed to SP, patients unable to take oral medication are given injectable or IV quinine until they are able to take tablets (personal

communications, Dr. Peter Kazembe, Dr. Brian Sharp). If, for example, an average of 2 days of injectable quinine were provided plus a full SP treatment dose, the full cost of the treatment would be Tsh 204 for under 5s and Tsh 1029 for over fives, significantly increasing the average cost per treatment for this group of patients.

Data are not available on either the current or future balance of formulations, but using some plausible assumptions, weighted average drug costs per treatment are shown in Table 3.2. Estimating that currently 60% of CQ treatments for under fives are provided as syrup, 30% as tablets and 10% as injections, the weighted average cost per first line treatment would be Tsh 41. Assuming that with the SP regimen, 90% of under five treatments would be tablets and 10% 2 days of quinine injections plus an SP treatment dose in tablets, the weighted average cost would fall to Tsh 25. For over fives, assuming that 90% of current CQ treatments are tablets and 10% injections, the current weighted average cost is Tsh 70. Changing to SP will not lead to cost savings from reduced use of syrup as this formulation is not generally used in this age group, but the cost of the injectable treatments will rise. If with the new regimen, 90% of treatments are SP tablets and 10% quinine injections and SP tablets, the weighted average cost would rise to Tsh 162. If 40% of suspected malaria out-patients are under five, the overall average cost per treatment would approximately double from Tsh 58 ($0.07) with CQ to Tsh 107 ($0.12) with SP. Better information is needed on the balance of forumulations currently used to refine these estimates[4].

Table 3.2 also shows the results of a one-way sensitivity analysis considering three factors which could reduce the weighted average first line drug cost with the SP regimen. Firstly, a substantial increase in the quantity of SP purchased is expected to lead to a fall in the unit price (personal communication, Christopher Msemo – Director of Procurement, MSD). If the price per tablet fell from the current rate of Tsh 20 to, for example, Tsh 15, the overall weighted average drug cost with SP would fall from Tsh 107 to Tsh 96 ($0.11). Secondly, although the Standard Treatment Guidelines state that CQ should be given orally whenever possible[(2)], there is some indication that injections are given when they are not strictly necessary, partly in response to demand from patients who may perceive injections as more effective[(18)]. If this were the case, there would be scope to reduce the percentage of first line therapies given in injectable form, which could lead to significant cost savings due to the high price of the quinine injections. For example, a reduction in the proportion of cases treated with injections from 10% to 5% would reduce the weighted average cost to Tsh 75 ($0.10) (using original

[4] Data available from Rufiji District for Jan-June 1999 provided the following breakdown of CQ formulations at peripheral facilities: Under fives – 69% tablets, 30% syrup, 1% injections; Over fives – 94% tablets, 1% syrup, 5% injections (Rufiji DHMT MTUHA and TEHIP Cost Information System (prototype)).

SP tablet price). Thirdly it is possible that as SP is increasingly adopted in Africa, the injectable form could be made available, avoiding the use of costly quinine injections as a first line therapy. For example, assuming that the price ratio between the tablet and injectable formulations would be the same as for CQ, a drug price per patient for injectable SP could be estimated at Tsh 30 for an under 5 and Tsh 180 for an over 5 (plus syringe). If the formulation were available at this price, the weighted average cost per treatment would fall to Tsh 46 ($0.06), less than the current weighted average cost with CQ.

### 3.3.3 The impact on expenditure on first line treatments

The impact of the change in regimen on expenditure on first line treatments can be calculated using the estimate of cases treated and the average drug cost per case (Table 3.2). Assuming that there are 7,7mn first line outpatient treatments per year, the first line drug costs with the CQ regimen are estimated at Tsh 446mn. Changing to the SP regimen with the baseline assumptions would increase the cost to Tsh 822mn, an annual increase of Tsh 376mn ($482,000). The sensitivity analysis shows that if the price of SP fell due to bulk purchase, the incremental cost would be Tsh 291mn, or if the proportion of treatments provided as injections was reduced to 5%, Tsh 130mn.

These figures should only be taken as a rough guide as, in the absence of good data on the number of outpatient visits, it was necessary to rely on very rough estimates of cases treated. As noted in Annex 2, there is a considerable discrepancy between the number of cases estimated from the MTUHA and the much higher figures supplied by MSD. MSD reported supplying 23mn antimalarial treatments a year, 88% of which were CQ, giving an estimate of approximately 20mn first line treatments. If these figures were more accurate than the estimates derived from MTUHA data, the true incremental cost of the new regimen would be roughly doubled. To provide more accurate budget predictions it will be essential to conduct an in depth investigation of current treatments provided.

## 3.4 Treatment cost savings

In addition to the incremental costs of changing the first line treatment, if drug efficacy improves, cost-savings, or “cost-offsets”, may arise due to reduced use of outpatient and inpatient drugs, and savings in other costs of treatment. The model estimates that with current failure rates with CQ, 11% of under-fives and 9% of over-fives would make a return visit to a formal outpatient or inpatient health facility. If a change were made to SP the model predicts that the return rate would be reduced to 5%

for under-fives and 0.1% for over-fives in the first year[5]. These cost-offsets may be subtracted from the gross cost of the intervention to estimate the net cost to the MOH.

### 3.4.1 Potential savings in outpatient drug costs

A reduction in the operational failure rate of the first line drug should reduce the need to provide outpatient drugs to patients making return visits (second and third line drugs and repeat prescriptions of the first line drug which is the only antimalarial available at PHC facilities). The impact on provider costs will depend on the return rate of patients with treatment failure to health facilities, and the change in the unit cost of second and third line treatments. With the proposed SP regimen the third line therapy will stay the same (oral quinine), but the second line will be changed from SP to the more costly amodiaquine (increase in drug cost per patient under 5 from Tsh 10 to Tsh 21).

### 3.4.2 Potential savings in inpatient drug costs

A reduction in the operational failure rate of the first line drug will reduce the number of cases becoming severe. Again the impact on provider costs will depend on the utilization rate for severe patients and the inpatient drugs provided. The Tanzanian Standard Treatment Guidelines recommend that patients admitted for malaria receive a 7 day course of quinine, in IV form until they can take it orally, followed by a treatment dose of SP[(2)]. In these calculations it has been assumed that patients receive on average 3 days IV and 4 days oral quinine, giving an average drug cost per admission of Tsh 965 for under 5s and Tsh 2,626 for over 5s.

### 3.4.3 Potential savings in other costs of inpatient and outpatient care

It is also possible that reducing the number of outpatient and inpatient cases will lead to savings in other, non-drug, costs of providing treatment. Table 3.3 shows data from a range of studies on the unit cost per inpatient and outpatient case (1999 prices). Two studies conducted in 1999 calculated malaria-specific unit costs, one on Mlimba Health Centre (full report of costing in Annex 4), and one on a range of facilities in Morogoro and Mbeya regions. The results of two older studies are also shown, which calculated general inpatient and outpatient unit costs (not malaria specific)[6]. The unit cost per outpatient visit ranged between Tsh 253 and Tsh 3,500 ($0.32 to $4.49), and the cost per inpatient admission between Tsh 2,380 and Tsh 39,710 ($3.05 to $50.91).

[5] By way of comparison, in Chipata, Kitwe and Lufwanyama Districts in Zambia in 1997,15% of children under five who had visited a clinic for fever or convulsions did so two or more times[(19)]. In 1995-6 total treatment failure with chloroquine was 42% in Chipata District and 39% in Lundazi District[(20)].

[6] In the near future results from the MTUHA/TEHIP Cost Information System in Morogoro Rural and Rufiji Districts will be available, providing routine data on the cost per case treated by age group and by disease in a sample of peripheral facilities, differentiated between initial and return visits.

The potential savings from averting a case will not be equal to the average cost of treatment because some proportion of the costs will be fixed, meaning that they will not vary with the number of patients. For example, analysis of the cost components of outpatient and inpatient visits at Mlimba Health Centre demonstrated that significant cost savings at this facility were very unlikely, as very few costs were expected to be variable (i.e. vary with utilization). Firstly, a change in patient numbers would not change the costs of buildings, equipment or administration. Secondly, as the Health Centre currently has 13 staff compared with a required establishment list of 21, it is very unlikely that there would be scope to reduce the number of staff. Finally, as other resources, such as drugs and laboratory consumables are in short supply and often run out before the end of the month, reducing the number of cases may not change consumption of these items either. It is possible that a higher proportion of costs would be variable in response to a very large change in patient numbers, but the impact on patient numbers is likely to be relatively low from a change in first line drug, which will mainly affect return rates, rather than the incidence of disease. It would therefore be misguided to expect large financial savings from reducing the number of return visits at PHC facilities. There may be greater potential for cost-savings at the hospital level if a significant number of inpatient admissions are averted, although this is likely to vary depending on the nature and utilization of the facility. Other studies have estimated that between 25% and 50% of hospital recurrent inpatient costs are variable[21, 22].

### 3.4.4 Calculating net costs

The decision tree model was used to estimate the net cost per patient with the two drug regimens, considering potential cost-savings in outpatient drugs, inpatient drugs and other facility costs (Table 3.4). No non-drug cost savings were included at PHC facilities. An estimated average cost per inpatient admission of Tsh 12,000 ($13.38) was used, and it was assumed that 75% of inpatient costs were recurrent, and 30% of recurrent costs were variable. Considering only the costs of the first line treatment and using baseline assumptions, changing to the SP regimen led to an increase in the average cost per patient in the year 2000 of Tsh 49. Including the impact on second and third line drugs reduced the differential to Tsh 46 per case, as the reduced number of return visits outweighed the higher unit cost per second line treatment. Including cost savings from reduced use of inpatient drugs reduced the differential to Tsh 35, and including cost savings from both drug and non-drug inpatient costs reduced the differential further to Tsh 9. These rough estimates imply that the potential cost-savings from providing more effective treatment would recoup over 80% of the incremental cost of providing a more expensive first line drug, reducing estimated incremental expenditure from Tsh 376mn to Tsh 67mn, even though relatively conservative assumptions about the potential for cost-

savings have been used. The maximum cost-savings will be observed immediately following the change in regimen in 2000. Over time as the difference between the efficacy of the two alternatives decreases, the potential for cost-savings will be reduced. For example comparing the two regimens in 2009, the incremental cost per patient of the SP regimen over the CQ regimen including all cost savings would be Tsh 33 (Tsh 25 using a 3% discount rate on costs). On average over the 5 year period the incremental net cost per patient would be Tsh 15, and over the 10 year period Tsh 23 (Tsh 14 and Tsh 20 respectively with a 3% discount rate).

Some of the provider cost-savings will be offset themselves by a corresponding fall in user fees. Whilst there are no official charges for children at Government PHC facilities, fees are in place for adults at PHC facilities and at hospitals, so a reduction in inpatient utilization would reduce provider revenue as well as costs. This has not been taken into account in the net cost calculations, but may be relatively insignificant if the proportion of costs currently covered by fees is relatively low. For example, Kilosa and Tukuyu District hospitals only recovered 6% of their recurrent costs through cost-sharing[23]. Moreover from a societal perspective, the reduction in user fees would represent a fall in revenue to Government but a saving to households.

As well as financial savings to providers from reducing the number of return visits, there could be other important benefits from reducing caseload. Firstly the quality of care may be improved, due to reductions in the frequency of drug and laboratory supply stockouts, less pressure on staff, and reduced patient waiting time. Secondly, costs to patients may be reduced through avoiding both return visits to formal health facilities, additional visits to other treatment sources, such as pharmacies, shops and traditional healers, and less time diverted from productive activities. Of the caretakers of children with suspected malaria visiting Mlimba Health Centre during an in vivo study of SP and Amodiaquine efficacy, 36% incurred some financial outlay over the course of the episode on drugs, other medical supplies, consultation fees, lab tests, stationery, transport and food. Overall average expenditure was Tsh 295 (including those who did not spend), half of which was for drugs. Over two thirds of the care takers spent more than 3 hours at the health facility, and 93% were unable to do their normal work that day (report attached as Annex 5). Most of the patients included in the Mlimba study received either Amodiaquine or SP, both of which have relatively high cure rates. It is not clear how much higher patient costs would have been if a less effective antimalarial, such as chloroquine, had been prescribed.

The analysis so far has assumed that the change in regimen will not have an impact on the initial number of cases seeking treatment. Whilst it is unlikely that there will be a significant change in

transmission and therefore incidence, it is possible that there could be important behavioural changes. There may be equilibrating tendencies with, for example, a reduction in utilization due to a fall in return visits leading to an increase in initial visits as patients become aware that waiting times and drug availability have improved. The outpatient utilization rate might increase if the new first line treatment is perceived to be more effective, or decrease if patients lose confidence when a familiar drug is replaced. Any of these changes could have an important effect on the predicted relative costs of the two regimens, and on the degree to which the public health care system meets the need of the population for care. In particular, concern has been raised that caretakers may perceive SP as less effective because it lacks the antipyretic effect of CQ, which could reduce utilization or necessitate the co-administration of an antipyretic agent such as paracetamol. However in a study in Zambia, SP was clearly perceived by caretakers as more efficacious than CQ, and the addition of paracetamol did not improve perceptions of its efficacy[24].

**Figure 3.1** Cost per treatment for a patient under five years of age with a range of antimalarials (1999 Tsh).

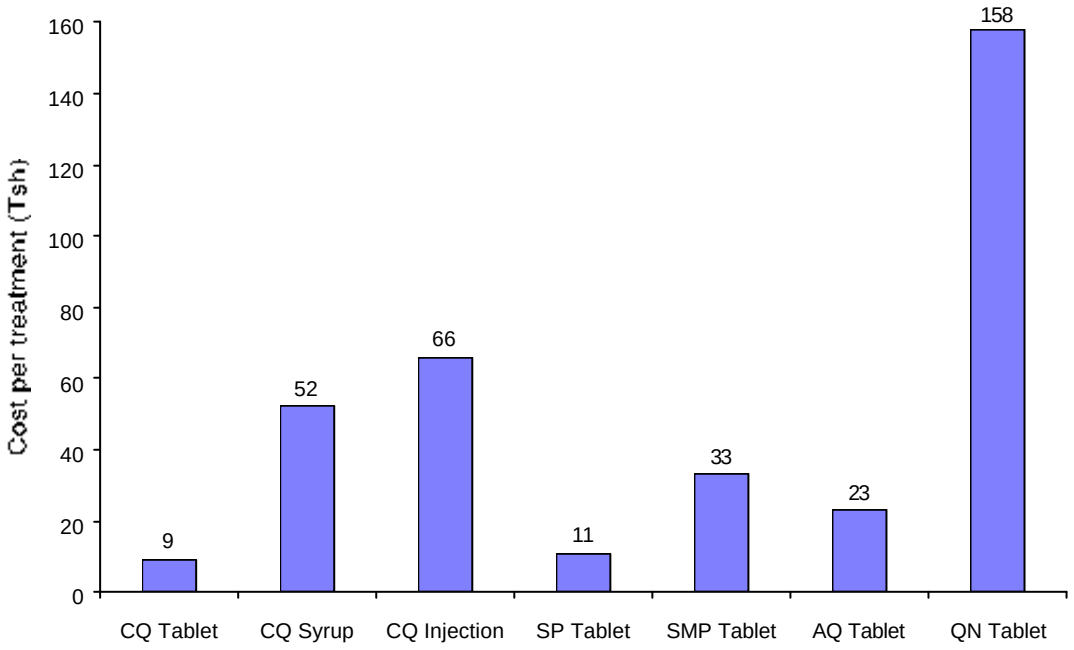


**Table 3.1** Average drug cost per treatment (1999 prices)

| Antimalarial | Formulation | Dose | Cost for patient under 5 years (average 10kg) | | Cost for patient over 5 years (average 60kg) | |
|---|---|---|---|---|---|---|
| | | | Tsh | US$ | Tsh | US$ |
| CQ | Tablet | 25mg/kg | 9 | 0.01 | 55 | 0.07 |
| | Syrup | 25mg/kg | 52 | 0.07 | n/a | n/a |
| | Injection | 25mg/kg | 66 | 0.08 | 204 | 0.26 |
| SP | Tablet | 25mg/kg | 11 | 0.01 | 66 | 0.08 |
| SMP | Tablet | 25mg/kg | 33 | 0.04 | 198 | 0.25 |
| Amodiaquine | Tablet | 25mg/kg | 23 | 0.03 | 138 | 0.18 |
| Quinine | Tablet | 2100mg/kg | 158 | 0.20 | 947 | 1.21 |
| | Injection | 2100mg/kg | 578 | 0.74 | 3273 | 4.20 |
| | IV | 2100mg/kg | 1172 | 1.50 | 3867 | 4.96 |

Notes
Drug prices from MSD catalogue, which already includes cost of distribution to districts[16], and International Drug Price Indicator Guide[17].
Cost of injection includes cost of syringe; cost of IV includes cost of IV kit, canula and dextrose.
10% wastage included for all drugs.

**Table 3.2** First line drug costs: average cost per treatment and total costs with the CQ and SP regimens (1999 prices)

| First Line Drug | Average cost per patient under 5 years | | Average cost per patient over 5 years | | Average cost per patient (all ages) | Total first line drug cost (7,7mn treatments p.a) |
|---|---|---|---|---|---|---|
| | Formulations | Average cost | Formulations | Average cost | | |
| CQ | 30% tablets<br>60% syrup<br>10% injection | Tsh 41<br>($0.05) | 90% tablet<br>10% injection | Tsh 70<br>($0.09) | Tsh 58<br>($0.07) | Tsh 446 mn<br>($572,000) |
| SP (baseline assumptions) | 90% tablets<br>10% QN injection<br>+ SP tablets | Tsh 25<br>($0.03) | 90% tablets<br>10% QN injection<br>+ SP tablets | Tsh 162<br>($0.21) | Tsh 107<br>($0.14) | Tsh 822mn<br>($1,054,000) |
| **One-way sensitivity analysis of weighted average cost of SP** | | | | | | |
| SP (with price per SP tablet reduced from Tsh 20 to Tsh 15) | 90% tablets<br>10% QN injection<br>+ SP tablets | Tsh 23<br>($0.03) | 90% tablets<br>10% QN injection<br>+ SP tablets | Tsh 146<br>($0.17) | Tsh 96<br>($0.11) | Tsh 737mn<br>($945,000) |
| SP (with % injections reduced from 10% to 5%) | 95% tablets<br>5% QN injection<br>+ SP tablets | Tsh 17<br>($0.02) | 95% tablets<br>5% QN injection<br>+ SP tablets | Tsh 114<br>($0.15) | Tsh 75<br>($0.10) | Tsh 576mn<br>($738,000) |
| SP (with SP injectable available at hypothetical cost of Tsh 30 for an under 5 and Tsh 180 for an over 5 + syringe) | 90% tablets<br>10% SP injections | Tsh 12<br>($0.02) | 90% tablets<br>10% SP injection | Tsh 69<br>($0.09) | Tsh 46<br>($0.06) | Tsh 353mn<br>($492,000) |

**Table 3.3** Provider unit costs of inpatient and outpatient care in Tanzania (1999 Tsh)

| Facilities covered | Year of Study | Unit Costs (Capital and Recurrent) |
|---|---|---|
| Mlimba Health Centre, Kilombero District (see Annex 4) | 1999 | Health Centre<br>Non-drug cost per outpatient visit with malaria diagnosis: Tsh 314<br>Non-drug cost per inpatient admission with malaria diagnosis (excluding drugs): Tsh 3,276 |
| 48 facilities in Morogoro and Mbeya Regions[23] | 1999 | Hospital / Health Centre / Dispensary<br>Full cost per outpatient visit for new case with diagnosis of malaria:<br>Under 5s: Tsh 2,690 / Tsh 1,200 / Tsh 1,230<br>Over 5s: Tsh 3,500 / Tsh 1,320 / Tsh 1,420<br>Full cost per inpatient admission with malaria diagnosis:<br>Under 5s: Tsh 16,610 / Tsh 2,380 / n/a<br>Over 5s: Tsh 16,040 / Tsh 2,800 / n/a |
| 4 District Hospitals [25] | 1993 | Hospital<br>Full cost per outpatient visit (not malaria specific): Tsh 450 – Tsh 2,264<br>Full cost per inpatient admission (not malaria specific): Tsh 8,072 – Tsh 39,710 |
| 58 facilities in Morogoro Region[21] | 1988/9 | Health Centre / Government Dispensary / Diocesan Dispensary<br>Full cost per curative outpatient visit (not malaria specific): Tsh 388 / Tsh 253 / Tsh 361<br>Full cost per inpatient admission (not malaria specific): Tsh 9,730 / n/a / Tsh 12,639 |

**Table 3.4** Gross and net costs per patient presenting with suspected malaria in the year 2000 (using baseline model assumptions) (1999 prices)

| Average cost per patient presenting with suspected malaria | CQ Regimen | SP Regimen | Incremental cost per patient | Total incremental cost (7,7mn initial treatments p.a.) |
|---|---|---|---|---|
| Cost of first line treatments | Tsh 58 ($0.07) | Tsh 107 ($0.14) | Tsh 49 ($0.06) | Tsh 376mn ($482,000) |
| Cost of first, second and third line outpatient drugs | Tsh 66 ($0.08) | Tsh 112 (0.14) | Tsh 46 ($0.06) | Tsh 350mn ($449,000) |
| Cost of first, second and third line outpatient drugs and inpatient drugs | Tsh 82 ($0.11) | Tsh 117 (0.15) | Tsh 35 (0.05) | Tsh 270mn ($346,000) |
| Cost of all drugs and other variable inpatient costs | Tsh 123 ($0.16) | Tsh 132 ($0.17) | Tsh 9 ($0.01) | Tsh 67mn ($86,000) |

# 4 Implementing the policy change of first line drug

## 4.1 Introduction

The appropriate introduction of new drugs is one of the greatest challenges to national malaria programmes. The process of policy implementation is a major task, requiring substantial funding, human resources, expertise, political will, and considerable time[26]. For example in Malawi, the process of planning and implementing the training, education and monitoring required for the introduction of SP took the Ministry of Health two years. The process is generally spearheaded by malaria and drug programme staff, but involves many stakeholders, ranging from top ministry officials, public health personnel, scientists, prescribers in private and public sectors, through to consumers.

Among the key factors required for successful implementation are:

- the provision of extensive information to both providers and consumers (WHO advises flooding providers and consumers with information)
- the inclusion of staff from peripheral formal facilities, as well as private sector practitioners and drug vendors in training programmes
- timing training and guideline distribution a short time ahead of the distribution of the new drug
- the timely procurement and distribution of adequate supplies of the new drug
- the development of a broad consensus behind the change among policy makers and health care workers.

Several consultative meetings have already taken place in Tanzania to establish the rationale for changing the current antimalarial treatment policy. A small group of stakeholders developed a summary report[3] that was discussed at the National Malaria Advisory Committee of the Ministry of Health. Endorsement of this document by the committee has initiated the process of policy review. The process involves direct consultations within the Ministry to get consensus at all levels. Furthermore, structures for strategic planning and implementation of the policy change have been put in place. Five committees were formed to oversee implementation, with members from the Ministry and its operational units, the scientific community, academia, Non-Governmental Organisations and the private sector. The responsibilities of the five committees were to review the treatment guidelines, organise SP procurement, review training curricula, establish operational/behavioural research on the

SP policy, and assess information-education-communication needs for public information on the policy change.

## 4.2 The costs of the policy change

Policy makers need information on the likely costs of this process, both for planning and budgeting purposes, and as an input into cost-effectiveness analysis. A detailed planning process involving Ministry staff and other stakeholders will be required to design an implementation strategy, but as a starting point for budget estimates an itemised costing was prepared as part of this study. It was envisaged that the process would involve 4 areas of activity: firstly consultation, consensus building and policy formulation, secondly revision and production of treatment guidelines, thirdly training of public and private sector health workers, and finally communication and publicity. Substantial management time and expertise will be required to effectively organise and undertake this wide range of activities, which may be a burden for already over-stretched Ministry staff. One possible approach would be to set up a full-time implementation team within the Ministry to take a lead role in the policy implementation, supplementing this capacity with local and international consultants where additional expertise was required. Alternatively the tasks could be added to the workload of a wider range of existing staff, but whatever strategy is chosen, it is important that the scope of activities to be implemented should not be underestimated.

As an example, the costing reported here includes a full-time implementation team for 18 months, consisting of 2 professional staff and 2 support staff, who would require a budget for office and vehicle expenses estimated at Tsh 85,5mn. In addition, Tsh 31,2mn has been budgeted for three 2-week consultancy visits at international rates. The four areas of activity are described in more detail below, and costed in Table 4.1.

It should be noted that activities involved in making the decision to change, as opposed to implementing the change once a decision has been reached, may also take considerable time and financial resources. Their costs have not been included in the estimates below.

**I. Consultation, consensus building and policy formulation**

Successful implementation requires consultation with a wide range of stakeholders to ensure that the process is appropriately designed and that individuals and organisations with key roles to play in implementation are supportive of the policy change. A series of meetings would be held of the advisory

board, the drug sensitivity task force (2 meetings each) and the task force sub-committee (5 meetings) to discuss policy issues, plan implementation, and prepare reports. Consultation with professional groups (e.g. Medical Association of Tanzania, Regional Medical Officers, Paediatric Association of Tanzania, etc.) could take place during their general meetings at limited extra cost, but it would be necessary to hold specific meetings to inform private practitioners and other stakeholders (one per zone).

Anecdotal evidence indicates that many health professionals working in facilities at district level or below are unaware of the extent of resistance to CQ and do not perceive an urgent need for change. This may be because patients with treatment failure often do not return to the facility where they were originally treated, and because it is difficult for health workers to distinguish failures due to resistance from those due to misdiagnosis or non-compliance. Experience from other countries has shown that the support of health workers at the periphery is vital to successful implementation of drug policy change. Consensus for change could be built by assisting key opinion leaders amongst health workers (such as district and regional medical officers) to undertake treatment failure studies to evaluate the extent and impact of chloroquine resistance in their areas. For example, a simple operational protocol could be used where a blood sample was taken from all patients with suspected malaria who were prescribed CQ, and the patients could be asked to make a return visit on day 7 to evaluate the extent of operational failure amongst those with parasitaemia on day 1. Resources for facilitators to assist in the implementation of 25 such studies around the country have been included in the costing. It is assumed that the results would be disseminated and discussed in regular District and Regional meetings. In total the activities falling under consultation, consensus building and policy formulation are estimated to cost Tsh 14,4mn.

**II. Development and production of treatment guidelines**

It will be necessary to revise and reprint both the Standard Treatment Guidelines for Tanzania and the Drug Use Guidelines for PHC Facilities. The budget includes a one-week workshop for the updating of the guidelines by a team of 6 people, and the production and distribution of 12,000 copies of the Standard Treatment Guidelines and 10,000 copies of the Drug Use Guidelines for PHC Facilities (total cost for development and production of Tsh 8,2mn).

**III. Training of public and private sector health workers**

It is necessary to ensure that staff at each health care facility are trained in the revised treatment policy. As there are over 5,000 health facilities in the country this represents a major task. In addition

community based health workers and private pharmacists, drug vendors or shopkeepers will also require training. A tiered system has been costed where a "training of trainers" (TOT) one-week workshop would be held to train 10 trainers. These trainers would then travel in pairs to each district to hold one-day training and sensitisation sessions for medical officers, pharmacists, nurses and hospital administrators for the district level, and separate sessions for health centre and dispensary staff. The aim would be to train at least one staff member from each facility (estimated total of 5,600 staff). In order to reach community based health workers, the national trainers would train 2 district level trainers, who would then go out to the field to train the village health workers and other allied staff, holding 10 meetings per district. Separate one-day sessions would be held in each district for private drug providers. Total training costs are estimated at Tsh 147,5mn.

### IV. Communication and Publicity

The provision and communication of information about the policy change is essential for its success. This will be done through a mix of strategies including printed and radio media channels. Costs have been estimated for the development, pre-testing and production of posters for general use in the community (60,000), posters for health facilities (20,000), leaflets (1,000,000) and a radio show. To publicise the change 4 press releases would be made with accompanying press conferences, and a one day media-sensitisation meeting would be held with journalists (total cost for communication and publicity of Tsh 44,1mn).

The total cost of implementing the policy change is estimated at Tsh 330,878,900 (US$ 424,204). The bulk of the costs are for training activities (45%) and the implementation team's expenses (26%). To put this in context, the total cost would be equivalent to around 3% of the MOH annual drugs budget, or 1% of the total annual MOH budget. It is possible that training costs could be reduced somewhat by piggy-backing drug policy training onto other on-going in-service training activities.

It is important to remember that the financial costs are only one measure of the burden of change, and that the costs in terms of staff time and managerial capacity should also be considered. In addition there are several other activities not included in the costing which will be required to support the process. Firstly the Essential Drug List will require revision, as AQ is not currently included, and secondly, drug regulations will have to be changed to allow SP to be provided at peripheral facilities. Following the change, post-marketing surveillance of drug quality, efficacy and safety will be essential. MSD will have to plan for drug procurement and distribution. Good management of the latter is essential to avoid the build up of excess stocks of CQ that would not be required after the change.

This will require considerable forward planning, as for example, in April 1999 MSD had stocks and outstanding orders for CQ for a consumption of 16-18 months[11]. MSD should be informed of any planned specifications and estimated consumption by July/August when they prepare their annual tenders for the EDP kits. In the event that a change were required more rapidly it might be possible to resell some CQ stocks to other countries where it is still useful.

**Table 4.1** Costs of policy implementation process (1999 Tsh)

**IMPLEMENTATION TEAM**

**Office Costs (4 people full time for 18 months)**

| | Number | Cost per Month | Number of months | Total Cost (Tsh) | % |
|---|---|---|---|---|---|
| Professional staff | 2 | 1000000 | 18 | 36,000,000 | |
| Support staff | 2 | 250000 | 18 | 9,000,000 | |
| Vehicle maintenance | | 500000 | 18 | 9,000,000 | |
| Office running costs | | 500000 | 18 | 9,000,000 | |
| | Number | Unit price | | | |
| Computer & printer | 1 | 2000000 | | 2,000,000 | |
| Office equipment | | | | 500,000 | |
| Vehicle | 1 | 20000000 | | 20,000,000 | |
| Sub-Total | | | | 85,500,000 | 26% |

**Consultancy**

| | | | | | |
|---|---|---|---|---|---|
| Various | | | | 31,200,000 | |
| Sub-Total | | | | 31,200,000 | 9% |

**ACTIVITY I: CONSULTATION, CONSENSUS BUILDING AND POLICY FORMULATION**

**Advisory board (2 meetings each for 40 people)**

| | Number of meetings | People per meeting | Cost per person | | | |
|---|---|---|---|---|---|---|
| Transport | 2 | 10 | 15000 | | 300,000 | |
| Honorarium | 2 | 30 | 10000 | | 600,000 | |
| Per diem | 2 | 10 | 60000 | | 1,200,000 | |
| Stationery | 2 | 40 | 1000 | | 80,000 | |
| | Number of meetings | People per meeting | Cost per sheet | Number of sheets | | |
| Production of reports | 2 | 40 | 40 | 6 | 19,200 | |
| Fuels | | | | | 12,500 | |
| Hall hire | | | | | 100,000 | |
| Sub-Total | | | | | 2,311,700 | 1% |

**Drug sensitivity task force (2 meetings for 21 persons)**

| | Number of meetings | People per meeting | Cost per person | | | |
|---|---|---|---|---|---|---|
| Transport | 2 | 10 | 40000 | | 800,000 | |
| Honorarium | 2 | 11 | 10000 | | 220,000 | |
| Per diem | 2 | 10 | 30000 | | 600,000 | |
| Stationery | 2 | 21 | 1000 | | 42,000 | |
| | Number of meetings | People per meeting | Cost per sheet | Number of sheets | | |
| Production of summary | 2 | 100 | 40 | 5 | 40,000 | |
| Production of report | 2 | 60 | 40 | 20 | 96,000 | |
| Fuels | | | | | 12,500 | |
| Hall hire | | | | | 100,000 | |
| Sub-Total | | | | | 1,910,500 | 1% |

**Sub-committee of Drug sensitivity task force (5 meetings for 8 persons)**

| | Number of meetings | People per meeting | Cost per person | | |
|---|---|---|---|---|---|
| Transport | 3 | 1 | 20000 | | 60,000 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Honorarium | 5 | 8 | 10000 | | 400,000 | |
| Per diem | 3 | 2 | 30000 | | 180,000 | |
| Stationery | 5 | 8 | 1000 | | 40,000 | |
| Production of reports | | | | | - | |
| Fuels | | | | | - | |
| Hall hire | | | | | - | |
| Sub-Total | | | | | 680,000 | 0.2% |

**Meetings for professional groups (to take place during their general meetings)**

| | Number of meetings | People per meeting | Cost per person | Number of days | | |
|---|---|---|---|---|---|---|
| Per diem | 5 | 2 | 30000 | 3 | 900,000 | |
| | Number of meetings | People per meeting | Cost per sheet | Number of sheets | | |
| Documents to distribute | 5 | 30 | 40 | 20 | 120,000 | |
| | Number of meetings | Cost per trip | | | | |
| Transport | 2 | 200000 | | | 400,000 | |
| Sub-Total | | | | | 1,420,000 | 0.4% |

**Private practitioners and other stakeholders**
**(one day meeting for 100 participants in four zonal Centres: Mbeya, Dar, Mwanza, Kilimanjaro)**

| | Number of meetings | People per meeting | Cost per person | Number of days | | |
|---|---|---|---|---|---|---|
| Per diem | 3 | 2 | 30000 | 3 | 540,000 | |
| Tea & coffee | 4 | 100 | 1500 | | 600,000 | |
| Stationery | 4 | 100 | 1000 | | 400,000 | |
| | Number of meetings | People per meeting | Cost per sheet | Number of sheets | | |
| Documents to distribute | 4 | 100 | 40 | 6 | 96,000 | |
| | Number of meetings | Cost per trip | | | | |
| Transport | 3 | 200000 | | | 600,000 | |
| Fuels | | | | | 12,500 | |
| Hall hire | | | | | 400,000 | |
| Sub-Total | | | | | 2,648,500 | 1% |

**Designing and facilitating treatment failure studies to build consensus for policy change (25 regional studies)**

| Workshop: | Number of people | Cost per person | Number of days | | | |
|---|---|---|---|---|---|---|
| Per diem | 6 | 30000 | 6 | | 1,080,000 | |
| Tea &coffee | 6 | 1500 | 5 | | 45,000 | |
| Fuels | | | | | 50,000 | |
| Stationery | | | | | 10,000 | |
| Regional Visits: | Number of meetings | Cost per person | Number of people | Number of days | | |
| Facilatators' transport | 25 | 20000 | 1 | | 500,000 | |
| Facilatators' per diem | 25 | 30000 | 1 | 5 | 3,750,000 | |
| Sub-Total | | | | | 5,435,000 | 2% |

**ACTIVITY II: REVISION AND PRODUCTION OF TREATMENT GUIDELINES**

**Revision of Treatment Guidelines (workshop for 6 people for 5 days)**

| | Number of people | Cost per person | Number of days | | |
|---|---|---|---|---|---|
| Per diem | 6 | 30000 | 6 | 1,080,000 | |
| Tea &coffee | 6 | 1500 | 5 | 45,000 | |

| | | | | | |
|---|---|---|---|---|---|
| Fuels | | | | 50,000 | |
| Stationery | | | | 10,000 | |
| Secretary | 1 | 20000 | 6 | 120,000 | |
| Driver | 1 | 20000 | 6 | 120,000 | |
| | | Cost per day | Number of days | | |
| Hall hire | | 30000 | 5 | 150,000 | |
| Sub-Total | | | | 1,575,000 | 0.5% |

**Production and Distribution of revised guidelines**

| | Number | unit cost | | |
|---|---|---|---|---|
| Standard Treatment Guidelines | 12000 | 300 | 3,600,000 | |
| PHC Facility Guidelines | 10000 | 300 | 3,000,000 | |
| Sub-Total | | | 6,600,000 | 2% |

**ACTIVITY III: TRAINING OF PUBLIC AND PRIVATE HEALTH WORKERS**

**Training of trainers (one week workshop in Dar es Salaam)**

| | Number of meetings | People per meeting | Cost per person | Number of days | |
|---|---|---|---|---|---|
| Per diem | 1 | 10 | 30000 | 7 | 2,100,000 |
| Tea &coffee | 1 | 24 | 1500 | 5 | 180,000 |
| Stationery | 1 | 24 | 1000 | | 24,000 |
| | Number of meetings | People per meeting | Cost per sheet | Number of sheets | |
| Documents to distribute | 1 | 24 | 40 | 20 | 19,200 |
| Fuels | | | | | 12,500 |
| Hall hire | | | | | 250,000 |
| Sub-Total | | | | | 2,585,700 |
| | | | | | 1% |

**Training/Sensitisation (150 Medical officers, 150 Pharmacists, 150 Nurses, 150 Hospital administrators)**

| | Number of people | Cost per person | Number of days | | |
|---|---|---|---|---|---|
| Per diem | 600 | 5000 | 1 | | 3,000,000 |
| Tea & coffee | 600 | 1500 | 1 | | 900,000 |
| Transport | 600 | 4000 | 1 | | 2,400,000 |
| Stationery | 600 | 1000 | 1 | | 600,000 |
| | Number of meetings | Cost per meeting | | | |
| Hall hire | 115 | 2000 | | | 230,000 |
| | Number of meetings | Cost per person | Number of people | Number of days | |
| Facilatators' transport | 115 | 20000 | 2 | | 4,600,000 |
| Facilatators' per diem | 115 | 30000 | 2 | 5 | 34,500,000 |
| Sub-Total | | | | | 46,230,000 |
| | | | | | 14% |

**Training/Sensitisation (Health Centre and Dispensary staff - 1 per facility, estimated total of 5000)**

| | Number of people | Cost per person | Number of days | |
|---|---|---|---|---|
| Transport | 5000 | 4000 | | 20,000,000 |
| Tea & coffee | 5000 | 1500 | | 7,500,000 |
| Per diem | 5000 | 5000 | | 25,000,000 |
| Stationery | 5000 | 1000 | | 5,000,000 |
| | Number of meetings | Cost per meeting | | |
| Hall hire | 115 | 2000 | | 230,000 |
| Sub-Total | | | | 57,730,000 |
| | | | | 17% |

**Private drug providers (one day meeting for 20 persons per district)**

| | Number of meetings | People per meeting | Cost per person | Number of days | | |
|---|---|---|---|---|---|---|
| Transport | 115 | 20 | 4000 | | 9,200,000 | |
| Tea&coffee | 115 | 40 | 1500 | | 6,900,000 | |
| Stationery | 115 | 40 | 1000 | | 4,600,000 | |
| | Number of meetings | Cost per meeting | | | | |
| Hall hire | 115 | 2000 | | | 230,000 | |
| Sub-Total | | | | | 20,930,000 | 6% |

**Training of trainers for community health workers**

| | Number of meetings | People per meeting | Cost per person | Number of days | | |
|---|---|---|---|---|---|---|
| Transport | 115 | 2 | 4000 | | 920,000 | |
| Tea & coffee | 115 | 2 | 1500 | 3 | 1,035,000 | |
| Per diem | 115 | 2 | 5000 | 5 | 5,750,000 | |
| Stationery | 115 | 2 | 1000 | | 230,000 | |
| | Number of regions | Cost per region | Number of days | | | |
| Fuels | 20 | 12500 | | | 250,000 | |
| Hall hire | 20 | 5000 | 3 | | 300,000 | |
| Sub-Total | | | | | 8,485,000 | 3% |

**Training of community based health workers**

| | Number of districts | Meetings per district | People per meeting | Cost per person | | |
|---|---|---|---|---|---|---|
| Transport | 115 | 10 | 2 | 4000 | 9,200,000 | |
| Stationery | 115 | 10 | 2 | 1000 | 2,300,000 | |
| Sub-Total | | | | | 11,500,000 | 3% |

**ACTIVITY IV: COMMUNICATION AND PUBLICITY**

**Design of IEC materials**

| | | | | | | |
|---|---|---|---|---|---|---|
| Development and pilot testing | | | | | 10,000,000 | |
| Sub-Total | | | | | 10,000,000 | 3% |

**Production and Distribution of IEC materials**

| | Number | unit cost | | | | |
|---|---|---|---|---|---|---|
| Posters for the community | 60000 | 100 | | | 6,000,000 | |
| Posters for the health facilities | 20000 | 100 | | | 2,000,000 | |
| Leaflets | 1000000 | 15 | | | 15,000,000 | |
| Sub-Total | | | | | 23,000,000 | 7% |

**Production of radio show**

| | | | | | | |
|---|---|---|---|---|---|---|
| Design and production | | | | | 10,000,000 | |
| Sub-Total | | | | | 10,000,000 | 3% |

**Media Sensitisation (one day meeting for 30 persons)**

| | Number of meetings | People per meeting | Cost per person | Number of days | | |
|---|---|---|---|---|---|---|
| Tea &coffee | 1 | 30 | 1500 | 1 | 45,000 | |
| Stationery | 1 | 30 | 1000 | 1 | 30,000 | |
| Fuels | | | | | 12,500 | |
| Hall hire | | | | | 50,000 | |
| Sub-Total | | | | | 137,500 | 0.04% |

**Press release for newspapers**

| | Number of releases | Cost per release | | |
|---|---|---|---|---|
| Press releases | 4 | 250000 | 1,000,000 | |
| Sub-Total | | | 1,000,000 | 0.3% |
| | | | | |
| **GRAND TOTAL** | | | **Tsh** | 100% |
| | | | **330,878,900** | |
| | | | **($424,204)** | |

# 5 Cost-effectiveness analysis

## 5.1 Methods for calculating cost-effectiveness

Cost-effectiveness analysis (CEA) provides a framework for the synthesis of data on epidemiological, behavioural, economic and managerial factors. Conducting a CEA involves identifying and measuring the costs and effectiveness of alternative strategies. The cost-effectiveness ratio is then calculated as the total incremental cost of an intervention divided by the number of units of health benefit.

The results of the analysis of the health impact and costs of the 2 regimens reported in Chapters 2 and 3 and the costs of implementation from Chapter 4 were combined to estimate the cost-effectiveness of the policy change. Two outcome measures were considered: the cost per operational failure averted, and the cost per death averted (with the latter being highly tentative due to the problems of estimating case fatality rates). A provider perspective was used, including only costs to the MOH (as discussed in Chapter 3, there may also be a significant impact on the costs to patients). All age groups were included, and two time frames were considered as described in Chapter 2: the 5 year period of 2000-2005, and the 10 year period 2000-2009. Incremental costs were included for all suspected malaria outpatients (including those incorrectly diagnosed), and a 3% discount rate was used for future costs.

## 5.2 Cost-effectiveness results

Baseline results are presented in Table 5.1 for three different cost definitions: firstly considering outpatient drug costs only (incorporating savings in second and third line outpatient drugs), secondly considering all drug costs (incorporating savings in all outpatient and inpatient drugs), and thirdly considering all costs (incorporating all drug and non-drug savings). Considering changes in outpatient drug costs only, using the SP regimen rather than the CQ regimen over the 10 year period would cost Tsh 362 ($0.46) per operational failure averted, or Tsh 26,000 ($32.85) per death averted. According to these results, the change in regimen would represent a highly cost-effective use of resources in comparison to other interventions to improve health. For example WHO has provided rough guidelines that any intervention with a cost per DALY averted under $25 would be considered a highly attractive use of resources[27], which would be very roughly equivalent to Tsh 390,000 or $500 per death averted[7]. If other cost-savings are included the switch appears even more cost-effective. For example,

[7] Assuming approximately 20 discounted years of life lost per death averted.

considering all drug and non-drug cost-savings the cost per operational failure averted would be Tsh 152 ($0.20), and the cost per death averted Tsh 11,000 ($13.82). If the regimens are compared over the 5, rather than 10-year time frame, all the cost-effectiveness ratios are slightly improved, as the difference between the effectiveness of the two regimens is greater during the first 5 years, as resistance to SP is assumed to grow faster than resistance to CQ. Moreover if the costs of the SP regimen were reduced as elaborated in Table 3.2 (for example by reducing the purchase price through bulk buying or reducing the proportion of treatments given as injections), the switch would appear even more cost-effective.

However, the results should be interpreted with caution. As highlighted in Chapters 2 and 3, the estimates of the effects and costs of changing regimen are subject to considerable uncertainty, and variability across regions. Figures 5.1 and 5.2 show the results of a one-way sensitivity analysis of the cost-effectiveness ratios (10 year time period, outpatient drug costs only). Changing individual parameters as specified in the figures varied the cost per operational failure averted between Tsh 314 and Tsh 817 ($0.40 and $1.05), and the cost per death averted between Tsh 26,000 and Tsh 81,000 ($32.85 and $103.68). It was not possible to calculate a cost-effectiveness ratio for the scenarios reported in Chapter 2 where the effects are negative, such as increasing the growth rate of resistance of SP relative to CQ to 6 times. Whilst from the baseline assumptions the change in policy appears a highly cost-effective way to improve health outcomes, given the high degree of uncertainty, one cannot completely rule out the possibility that the impact of the change on health outcomes could be negative.

It is also important to remember that the outcome of a CEA depends on the choice of options compared. This analysis is restricted to a comparison of CQ and SP regimens over a 5 or 10 year period. It does not consider the likely effects or costs beyond 10 years, nor does it consider other treatment options that may become available, such as chloroproguanil-dapsone (Lapdap), or a combination therapy of SP or Lapdap with an artemisinin derivative. Moreover the analysis does not take into account that introducing SP as first line, and as a result increasing the growth rate of SP resistance, could compromise the potential efficacy of these alternative options. This is a cause for concern as it is anticipated that there will be cross-resistance between SP and Lapdap, and experience in South East Asia suggests that combination therapies may be more effective at slowing the development of resistance when initial resistance levels to both drugs are relatively low[28, 29].

Finally, changing the first line drug is not the only way to improve malaria case management. Many other strategies may be used to improve the quality of care and the effectiveness of therapy. For

example, analysis using the decision tree model for an African context has shown that using pre-packaging of drugs and education to improve compliance, and increasing the availability of second and third line therapies at peripheral facilities are both likely to be highly cost-effective strategies[30].

**Figure 5.1** One-way sensitivity analysis of the cost per operational failure averted by changing from the CQ to the SP regimen (all ages, outpatient drug costs only, over the 10 year time period) (Tsh 1999)

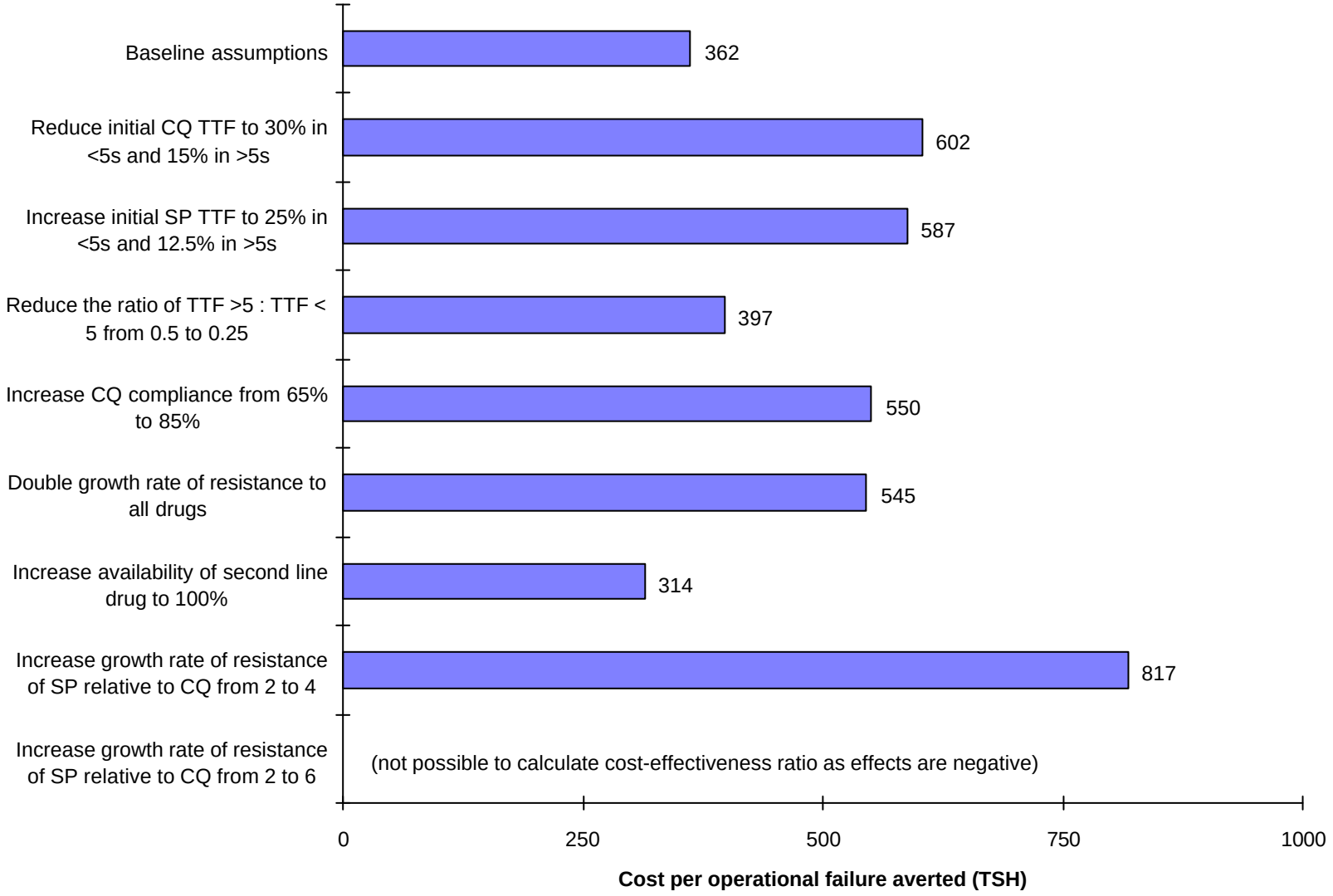


**Figure 5.2** One-way sensitivity analysis of the cost per death averted by changing from the CQ to the SP regimen (all ages, outpatient drug costs only, over the 10 year time period) (Tsh 1999)

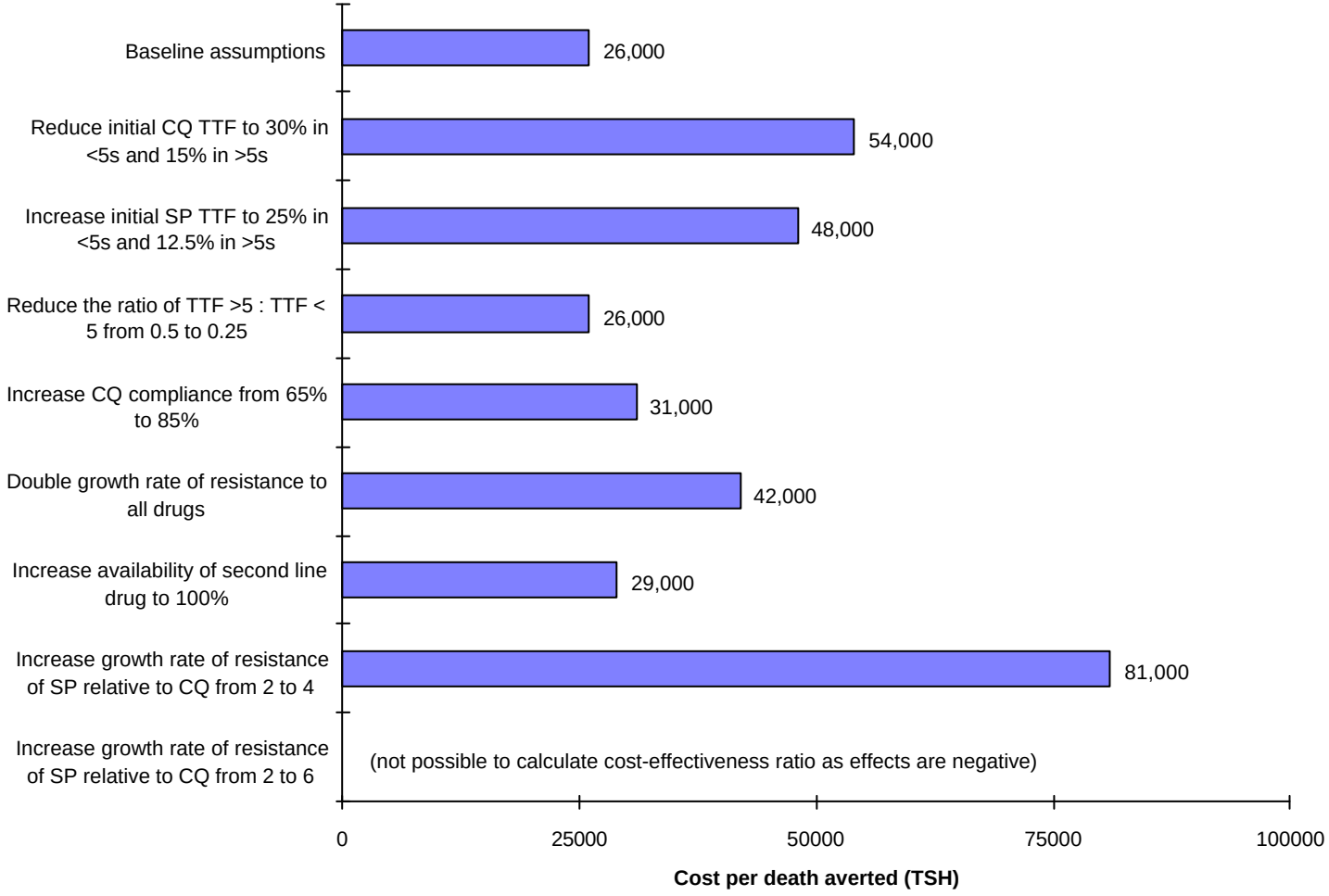


**Table 5.1** Cost-effectiveness of SP regimen compared to CQ regimen (all ages, using baseline model assumptions) (1999 prices)

| | Over 5 year time period | | Over 10 year time period | |
|---|---|---|---|---|
| | Cost per operational failure averted | Cost per death averted | Cost per operational failure averted | Cost per death averted |
| Considering outpatient drug costs only (incorporating savings in second and third line outpatient drugs) | Tsh 345 ($0.44) | Tsh 24,000 ($30.49) | Tsh 362 ($0.46) | Tsh 26,000 ($32.85) |
| Considering all drug costs (incorporating savings in all outpatient and inpatient drugs) | Tsh 281 ($0.36) | Tsh 19,000 (24.82) | Tsh 302 ($0.39) | Tsh 21,000 (27.45) |
| Considering all costs (incorporating all drug and non-drug savings) | Tsh 118 ($0.15) | Tsh 8,000 ($10.47) | Tsh 152 ($0.20) | Tsh 11,000 ($13.82) |

# 6 Conclusions

1. At current levels of drug resistance, health outcomes in terms of operational treatment failures, number of severe cases and deaths would be significantly better with SP as the first line drug. This is because data from sentinel sites show that drug efficacy is much higher with SP, compliance is expected to be higher, and treatment failure often results in the development of severe disease.

2. Allowing for the growth of drug resistance over time, and assuming that resistance will grow twice as fast to SP than to CQ as first line drugs, health outcomes would be significantly better on average using SP as first line over the next 5 years, or over the next 10 years. This conclusion is robust to changes in most parameters over reasonable ranges, although given the high levels of uncertainty involved, one cannot completely rule out the possibility that health outcomes would be better with CQ.

3. The costs of first line treatment for the Ministry are dependent both on the choice of drug and the mix of formulations used. The cost per treatment is similar for CQ and SP tablets, and a reduction in the use of a syrup formulation could lead to substantial savings. However it is unclear what drug will be used for cases previously treated with CQ injections, as SP injectables are not available. If quinine injections were used instead, the overall costs of first line treatment would substantially increase.

4. Reducing treatment failures with the first line drug could lead to significant savings in second and third line drugs, and the costs of inpatient treatment. Baseline estimates indicate that in the first year of the new regimen, cost-savings could recoup over 80% of the incremental cost of the new regimen. Over time the potential for cost-savings would be reduced as the difference between the efficacy of the two alternatives decreased.

5. The process of policy implementation is a major task, requiring substantial funding, human resources, expertise, political will, and considerable time. The activities involved include consultation, consensus building and policy formulation, revision and production of treatment guidelines, training of public and private sector health workers, and communication and publicity, and are estimated to cost around Tsh 331mn ($424,000).

6. Using the baseline assumptions, the change in policy to the SP regimen appears a highly cost-

effective way to improve health outcomes. However, the results should be interpreted with caution, given the high degree of uncertainty involved, and the potential impact of higher SP resistance on future treatment strategies (such as combination therapy) which have not been incorporated in the analysis.

7. The analysis has highlighted several key gaps in information available for drug policy:

- Treatment failure rates for patients over 5 years. The lack of this information is a major constraint on the estimation of the health impact of the current or proposed regimens and needs to be collected as a priority[8]. In the past the focus has been on under 5s as it is argued that the burden of disease is overwhelmingly concentrated in this age group. Whilst it is true that this age group has by far the highest death rate, malaria is also an important cause of morbidity and mortality in people over 5 years of age. Patients over 5 years of age make up 60% of all outpatients with suspected malaria, and around half the reported inpatient malaria deaths in Tanzania (1).
- Treatment seeking behaviour. It was necessary to base the analysis on average estimates of the probability of seeking treatment from elsewhere in Africa. Given the adverse health consequence of treatment failure, it is particularly important that these behavioural data are collected on treatment seeking practices for failures with both uncomplicated and severe disease.
- The number of antimalarial treatments currently provided in the public sector and the mix of formulations used. There is a considerable difference between the reported number of treatments supplied by MSD, and the much lower number of cases reported in the MTUHA (even scaled up for under-reporting). This presents many difficulties for the estimation of the costs of changing regimen. Further investigation to explore this discrepancy is essential in order to assess whether the current estimates are appropriate.
- The number and type of antimalarial treatments provided by the private sector (including clinics, pharmacies, shops and traders). Very little is known about the provision of antimalarials in the private sector, but several studies have shown that it is an important source, and is therefore likely to have a significant effect on both current cure rates and the development of drug resistance over time.
- Investigation of the most efficient way to treat patients who cannot take oral medication if SP becomes the first line drug.

[8] A study is currently underway to collect data on clinical failure at health centres for a range of age groups based on passive case detection – PI Dr. Zul Premji, Muhimbili Medical Centre.

- The probability of developing severe malaria with early and late treatment failure. The findings from Mlimba Health Centre of a substantial differential between the risk of developing severe disease with early and late treatment failure warrant further investigation. The relative risk should be explored for a range of drugs and at a variety of resistance levels.
- The process of policy change. Where a change in treatment regimen is implemented in Africa, the process should be carefully documented and costed as an aid for other countries planning to change policy.

# Annexes

**Annex 1:** Model structure, input variables and data sources

**Annex 2:** How many malaria outpatient visits are there in Tanzania?

**Annex 3:** Report on Health Seeking Behaviour and Antimalarial Treatment in Tanzania

**Annex 4:** The provider costs of treating malaria patients at Mlimba Health Centre

**Annex 5:** Use of antimalarials and the costs of seeking care for presumptive malaria in children attending for care at Mlimba Health Centre

## Annex 1: Detailed Description of Decision Tree Model

***Model Structure***

The outcome of treatment for people presenting at an outpatient facility with suspected uncomplicated malaria was modelled using the decision tree depicted in Annex 1 Figure 1. Patients enter the tree at point A, when they are given the first line drug. Due to the use of clinical diagnosis, a large proportion of these patients may not actually be suffering from malaria. The outcomes for these false positive cases were not calculated as they were assumed to be unaffected by a change in the antimalarial used. Of those who are suffering from malaria, there may be cure or failure with the first line drug depending on both drug efficacy and compliance. Given that the first line drug has failed, the patient will either develop severe malaria, or continue to suffer from uncomplicated malaria. If severe malaria develops, formal[9] inpatient care may be sought (public or private), when the patient will receive intravenous quinine. The probability is then estimated of recovery and death with inpatient care and without inpatient care.

If the patient still has uncomplicated malaria after failing with the first line drug, he or she may choose to seek further formal outpatient care, where in the absence of a drug stock out, they will be given another treatment course. In the event of a failure following this second visit, it is again possible that severe malaria will develop, or that uncomplicated malaria will persist. If severe malaria develops, patients may or may not seek formal inpatient care, as described above. If uncomplicated malaria persists, patients will again decide whether to attend outpatients, and if they do will be given a third treatment course. If there is treatment failure following the third visit, patients will either ultimately recover or die. The risk of lethal side-effects was not included, because the estimated rates are so low that they do not make any significant difference to the model results.

The decision tree was used to calculate the probability of an outpatient with malaria entering the system experiencing:

- operational failure following the first outpatient visit (which is a function of both TTF and non-compliance)
- developing severe malaria during this episode (including those that do not return to a facility)
- inpatient admission during this episode
- death as a result of this episode.

[9] Formal facilities are defined as public, private commercial and not-for-profit registered health facilities with appropriately trained staff.

These outcomes were calculated in each year from 2000 to 2009 for two scenarios: firstly maintaining the CQ regimen, and secondly changing to the SP regimen in 2000 and using this regimen for the subsequent 9 years.

***Probability estimates***

Estimates for each of the probabilities in the decision tree were drawn from a review of published and unpublished data from Tanzania and other African countries. The estimates and sources used for the probabilities in the decision tree are documented in Annex 1 Table 1. Estimates were made separately for patients over and under 5 years of age, assuming that 40% of outpatients with suspected malaria were under 5[1].

The probability that the suspected episode was caused by malaria was estimated as 0.46, based on the average of a range of studies on the accuracy of clinical diagnosis for malaria in Africa[31-35].

The probability of failure with an outpatient drug was defined as

Probability of Failure = 1 - (Cure Rate x Compliance Rate)

where the cure rate refers to the "adequate clinical response rate" (ACR). "Resistance" is defined as total treatment failure (TTF) or (1-ACR). Response to treatment was defined as treatment failure if by day 14 the patient had parasitaemia and a temperature higher than 37.5°C[8]. Estimates for the current ACR with CQ, SP and amodiaquine were based on recent data on TTF in children under five years from sentinel sites. TTF rates were estimated using the national sentinel antimalarial monitoring procedures for recruitment and determining treatment response[8]. Current TTF with each drug was approximated as the mean of the available estimates, giving an initial TTF of 50% for CQ, 14% for SP and 5% for amodiaquine. (There is considerable variation in resistance levels across Tanzania, and averaging the available estimates may not provide representative estimates.) In the absence of data on treatment failure rates for patients over 5 years of age a rough estimate was made that the rate of TTF in patients over 5 years of age would be half that in patients under 5. In areas of stable endemicity, one would expect lower failure rates in higher age groups, as older patients are more likely to exhibit acquired immunity.

Compliance was defined as receiving at least the minimum required dose. Compliance with treatment therapy is very difficult to measure accurately and few studies are available. Estimates of compliance were made from data collected on patients at Mlimba Health Centre, from other estimates reported in

the literature[36] and discussions with experts (see Annex 3). Data were collected at Mlimba Health Centre on reported compliance in "unsupervised" patients of 84% with amodiaquine and 90% with SP (Abdulla, unpublished report). However, as these patients were expecting to be visited on day 3, their compliance is likely to have been higher than normal. These figures could therefore be considered as the upper limit of compliance with these drugs. Estimates were therefore made of 65% with CQ and amodiaquine, 88% with SP and 40% with oral quinine. One would expect compliance to be highest with SP which is taken in a single dose, and lowest with oral quinine, which has to be taken over 7 days and has unpleasant minor side-effects.

In some cases of non-compliance with multiple dose drugs only minor under-dosing will occur, which may still have some therapeutic effect. In the absence of drug resistance, it was therefore assumed that under-dosing with multi-dose drugs would be effective in 20% of cases under-dosed. Under-dosing with a single dose drug, such as SP, was assumed to have zero effectiveness (although it is possible that adult patients could take less than 3 tablets of the single dose and still experience some benefit).

The probability of developing severe disease following a treatment failure for children under 5 years in the Mlimba Health Centre study was 30% with early treatment failure (ETF) and 4.3% with late treatment failure (LTF). These data are underestimates for an operational situation, as the patients were followed up over a two week period and treated if they had clinical failure or more than 25% of the initial parasite load, which would have prevented progression to severe disease in some patients. The proportion of all treatment failures which are ETF was held constant at 43%, the overall average rate for all drugs tested at the sentinel sites, giving a weighted probability of becoming severe following any failure of 15.4% in patients under 5. No data were available on patients over 5 years, so an overall estimate was made that 1% of all treatment failures would become severe. Further investigation is needed of how the ratio of ETF:LTF varies at different rates of overall TTF, and with different drugs, and on the consequences of treatment failure in patients over 5 years of age.

The probability of becoming severe following first line failure was adjusted according to the probability of returning to a formal public or private outpatient facility. With 100% failures treated again, the probability of becoming severe is taken to be the same as that calculated from the Mlimba study. With no treatment of failures it was assumed that the probability of becoming severe increases by 50%. A linear relationship was assumed between level of repeat treatment and probability of becoming severe.

For patients that fail first line drug, remain uncomplicated by day 14 and do not seek further outpatient care, the probability of developing severe malaria is assumed to be a third of the probability of developing severe malaria within 14 days of first line failure. The probability of recovery and death was assumed to be the same for all those with severe malaria not seeking formal treatment, which includes those who use self-treatment, or traditional medicine and those who do nothing. This is unlikely to hold if some patients are obtaining effective over-the-counter drugs, but in the absence of effectiveness data it was not possible to estimate its impact.

Of those with treatment failure who remained uncomplicated, it was estimated that 48% would return to a formal public or private outpatient facility, based on the average rate of formal facility utilization in Africa from a review of treatment seeking behaviour for malaria by McCombie, 1996[37]. However not all returning patients will receive an additional drug. Drug stockouts frequently occur at peripheral facilities as the EDP kit often does not last the whole month[13-15]. The true frequency of drug stockouts was not known, so it was estimated that antimalarials would not be available for 15% of outpatient visits. However, as it is common for patients and caretakers experiencing stockouts to purchase the recommended drugs from commercial outlets instead[15], it was assumed that 66% of patients experiencing a stock out would purchase the prescribed drugs over the counter. (The costs of purchasing these drugs over the counter are not included in provider costs.)

In Tanzania the official second line treatment is generally only available at hospitals, so it was assumed that if a patient returned to a health centre or dispensary they would be given the first line again, and only if their second visit was to a hospital outpatient department would they be given the second line drug. The probability of receiving the second line on a return visit was therefore set equal to the proportion of suspected malaria outpatient visits that take place at hospital (10% - based on MTUHA figures adjusted upwards to include referral hospitals). Where the same first line drug was prescribed again it was assumed that all patients who had failed following their first visit due to parasite resistance to the first line drug would automatically fail again, and only those failures due to non-compliance would have a chance of a cure with the repeat prescription.

Of those with treatment failure who became severe, it was estimated that 48% would be admitted to a formal public or private inpatient facility, again based on the average formal facility utilization from the review by McCombie, 1996[37][10]. The case fatality rates for inpatients with severe malaria were taken

[10] In the absence of detailed information the probability of seeking care following treatment failure was assumed to be the same for uncomplicated and severe disease. However, one might expect the probability to be higher for more severe disease if it is perceived as more urgent, or lower if severe disease is less likely to be perceived as

from the MTUHA as 2.9% in under 5s and 2.4% in over 5s. No data are available on case fatality rates for severe cases which do not receive inpatient care, so very rough estimates of 15% in under 5s and 7% in over 5s were made.

***Modelling the growth of drug resistance***

The growth of drug resistance over time was modelled as a logistic growth function. If $R_{i,t}$ is the level of resistance to drug $i$ at time $t$, the rate of increase in drug resistance over time $t$ is given by the logistic equation,

$$\frac{dR_i}{dt} = r_i R_{i,0}\left(1 - \frac{R_{i,0}}{K_i}\right),$$

*equation 1*

where $R_{i,0}$ is the starting level of drug resistance at time $t$=0, $K_i$ is the maximum potential level of resistance to drug $i$, and $r_i$ is the maximum growth rate of resistance to drug $i$ (which is approached when $R_i$ is very small relative to $K_i$). Equation 1 may be solved to give an analytical expression for $R_i$ at any time $t$

$$R_{i,t} = K_i\left(\frac{R_{i,0}}{R_{i,0} + (K_i - R_{i,0})e^{-r_i t}}\right),$$

*equation 2*

Equation 2 can be rearranged to show that the time taken to reach 0.5 resistance is inversely proportional to $r_i$, and if $r_i$ is doubled then this time is halved.

An estimate of the growth rate of resistance to CQ when used as a first line drug was made by fitting the logistic growth model subject to the constraints that $R_{CQ,1950}$ was 0.025 and $R_{CQ,1999}$ was 0.5, based on the historical point estimates of CQ resistance provided by the Tanzanian Ministry of Health Task Force on Antimalarial Drug Policy from 1950 to 1999. As very few data points were available, the study sites were not representative and methods not comparable, these point estimates must be considered as highly approximate. It was assumed that $K_{CQ}$ equalled 1. This provided an estimate for $r_{CQ}$ of 0.12. The historical point estimates and fitted growth model are shown in Figure 2.1 (Chapter 2).

There is very little evidence on the growth rates of resistance to other drugs in Africa, so estimates were made based on the characteristics of the drugs, and their role in the official regimen. If SP were

---

having a bio-medical cause (See Annex 3 on Health Seeking Behaviour).

adopted as the first line drug, it is expected that resistance would grow more quickly than to CQ, due to the longer half-life of SP and the drug-specific mechanisms underlying the development of resistance[38, 39]. As an approximation $r_{SP}$ was assumed to be twice $r_{CQ}$ (i.e. $r_{SP} = 0.24$). Resistance to amodiaquine as a first line drug (not used in model) was assumed to increase at 1.5 times resistance to CQ as a first line drug ($r_{AQ} = 0.18$). Although amodiaquine is similar in many of its characteristics to CQ, there is likely to be some cross-resistance mechanisms operating between the two drugs, leading one to expect resistance to amodiaquine to appear more rapidly in areas where CQ resistance is already high. When any drug was used as a second line, resistance was assumed to increase at only 33% of its rate of growth as a first line drug ($r_{SP} = 0.08$, $r_{AQ} = 0.06$ ), as it would be much less widely used, and the prevalence of drug use has theoretically been shown to be the most important factor in determining the rate of spread of resistance[40]. As resistance to quinine has remained low despite its widespread use as a referral drug, the growth of resistance to quinine as a third line drug and treatment for severe malaria was assumed to be zero.

***Limitations***

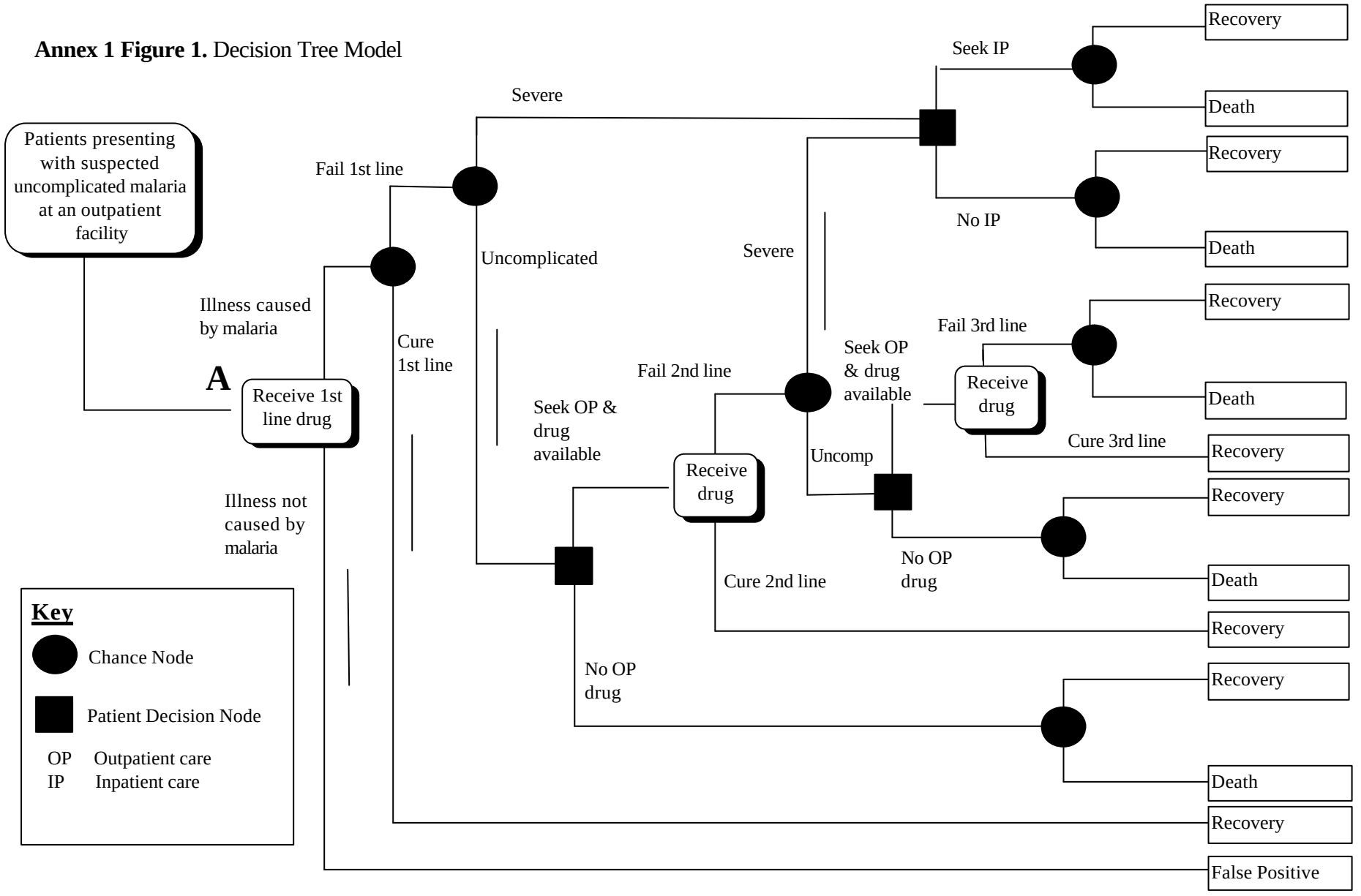
Developing a model of this kind inevitably involves considerable reliance on highly uncertain input parameter estimates. The implications of varying key inputs are explored in the one-way and multi-way sensitivity analyses in the main text. However this does not fully capture all uncertainty, especially uncertainty in the model structure. Several limitations should be noted:

- The model captures only the impact of drug resistance on uncomplicated and severe febrile illness, excluding any effects on other health impacts of malaria such as chronic anaemia, low birth weight, or neurological sequelae resulting from severe episodes.
- The model is a fairly crude representation of the complex patterns of treatment seeking behaviour that occur in practice. Treatment is modelled as a linear progression through a series of stages, but in reality care-seeking pathways tend to be highly varied[41]. Patients may alternate between formal and informal providers, and may use more than one source of care at the same time.
- The model is based on a given population of patients seeking outpatient care, but it is possible that a change in drug regimen could lead to a change in the outpatient utilization rate, either causing an increase if treatment is perceived to be more effective, or a decrease if patients lose confidence when a long-familiar drug is replaced[24].
- The definition of TTF covers treatment failure up to day 14 following the start of treatment. In areas of high transmission a certain proportion of day 14 positives will be re-infections, rather than failures, especially with short half-life drugs.

- Severe malaria as a result of treatment failure is defined as a case which would warrant inpatient admission if it were to present at a health facility. It should be noted that the definition of severe disease would be likely to vary from place to place.
- Predicted growth rates of resistance are highly speculative, as the empirical evidence on the development of SP resistance is very mixed. For example, in Thailand, following the replacement of CQ with SP as the first line treatment SP cure rates fell from over 80% to under 20% in five years[42]. However, in Malawi although SP was adopted as first line drug in 1993, significant increases in clinical failure are yet to be recorded. However the experience might be expected to be different in Tanzania, as initial levels of SP resistance were much lower in Malawi at the time of switch[43]. A more rapid year-on-year increase in SP resistance might therefore be anticipated in Tanzania.
- It was assumed that the rates of growth of drug resistance depended on the role of the drug in the official regimen. This may over-emphasize the importance of the public sector in drug distribution in some countries. On average between 40% and 60% of antimalarials in SSA are distributed through private providers[44] and, if a drug becomes widely available in the private sector, resistance may grow rapidly, even when it is not part of the official regimen.

All of these limitations should be borne in mind in interpreting the model's results.

**Annex 1 Figure 1.** Decision Tree Model



**Annex 1 Table 1.** Input variables used in the decision tree model.

(Where no source is given data were not available and the estimates are based on discussions with researchers in the field.)

| Model input variable | Best estimate | Estimates used in sensitivity analysis | Source |
|---|---|---|---|
| **Suspected outpatient case is caused by malaria** | 0.46 | | Based on review of African literature on the accuracy of clinical diagnosis [31-35] |
| **Drug stockout at outpatients** | 0.15 | | |
| **Initial adequate clinical response rate (ACR) in <5s:** | | | |
| CQ | 0.50 | 0.60, 0.70 | Sentinel site data (unpublished) |
| SP | 0.86 | 0.75 | Sentinel site data (unpublished) |
| Amodiaquine | 0.95 | | Sentinel site data (unpublished) |
| Quinine | 1.00 | | Expert opinion |
| **Initial adequate clinical response rate (ACR) in >5s:** | | | |
| CQ | 0.75 | 0.80, 0.85, 0.88 | Approximated assuming that the TTF in >5s will be half the TTF in |
| SP | 0.93 | 0.88, 0.97 | <5s |
| Amodiaquine | 0.98 | 0.99 | |
| Quinine | 1.00 | | |
| **Compliance:** | | | |
| CQ | 0.65 | 0.85 | Mlimba Health Centre data, Slutsker *et al.*, 1994[36], |
| SP | 0.88 | | |
| Amodiaquine | 0.65 | | |
| Quinine | 0.40 | | |

| Model input variable | Best estimate | Estimates used in sensitivity analysis | Source |
|---|---|---|---|
| **Non-compliers for whom treatment is effective:** | | | |
| CQ | 0.2 | | |
| SP | 0 | | |
| Quinine | 0.2 | | |
| Amodiaquine | 0.2 | | |
| **Develop severe malaria if ETF:** | | | |
| age <5 | 0.300 | | Mlimba Health Centre study data (Abdulla, unpublished) |
| age >5 | 0.010 | | |
| **Develop severe malaria if LTF:** | | | |
| age <5 | 0.043 | | Mlimba Health Centre study data (Abdulla, unpublished) |
| age >5 | 0.010 | | |
| **Proportion of TTF that are ETF** | 0.43 | | Average for all drugs from sentinel site data |
| **Seek outpatient care if treatment failure and uncomplicated** | 0.48 | | Average from review of treatment seeking behaviour by McCombie, 1996[37] |
| **Seek inpatient care if treatment failure and severe** | 0.48 | | Average from review of treatment seeking behaviour by McCombie, 1996[37] |
| **Case fatality rate if seek formal inpatient care:** | | | |
| age <5 | 0.029 | | MTUHA 1996 – CFR for severe malaria inpatients[1] |
| age >5 | 0.024 | | |

| Model input variable | Best estimate | Estimates used in sensitivity analysis | Source |
|---|---|---|---|
| **Case fatality rate if severe and do not seek formal inpatient: care** | | | |
| age <5 | 0.15 | 0.10, 0.30 | |
| age >5 | 0.07 | 0.05, 0.15 | |
| **Proportion of outpatient cases <5 years of age** | 0.4 | | MTUHA 1996 – proportion of all outpatient visits for suspected malaria which are for <5s[1] |
| **Proportion of return visits where second line drug is available** | 0.06 | 1.00 | Based on proportion of outpatient cases which are at hospital MTUHA 1996[1] |
| ***r* value for the growth rate of resistance to drugs as first line therapy:** | | | |
| CQ | 0.12 | 0.24 | |
| SP | 0.24 | 0.36, 0.48, 0.72, 0.96 | |

## Annex 2: How many malaria outpatient visits are there in Tanzania?

This seemingly simple question is actually very difficult to answer. Information on suspected malaria cases should be collected for all public and private health facilities through Tanzania's Health Management Information System (HMIS, or MTUHA). However, the MTUHA is relatively new, having only reached nationwide coverage at the start of 1996. Data entry for 1998 is not yet finished, and the records from 1997 are very incomplete due to the exceptionally adverse weather conditions. Currently the only usable data are therefore for 1996 and, even in this year, the reporting rate for Annual Health Facility OPD was only 51%. In addition the 1996 MTUHA data do not include patients seen at Tanzania's four referral hospitals. In 1996 the MTUHA reported 4,9mn outpatient diagnoses of malaria (see Annex 2 Table 1). Scaling up proportionately for under-reporting gives an estimated total of 9,6mn. As a rough approximation, this could be rounded up to 10mn per year including referral hospitals.

To calculate the cost and health outcome estimates in the report, data are needed on the number of initial outpatient visits for malaria (i.e. first visits for a given episode). The decision tree model was used to estimate the ratio between initial and return visits based on the probabilities of current operational failure, becoming severe, and making a return visit, leading to an estimate that 91% of outpatient visits for suspected malaria would be initial visits, or 9,1mn per year.

By far the majority of these cases would be diagnosed purely on the basis of clinical symptoms. There is likely to be a high level of over-diagnosis, as in endemic areas the symptoms of malaria are difficult to distinguish from several other common causes of febrile disease. Assuming that 46% of clinically diagnosed episodes were actually caused by malaria (based on the average of a range of studies on the accuracy of clinical diagnosis for malaria in Africa[31-35]), the estimated number of true malaria outpatient cases per year would be 4,4mn, 4,0mn of which would be initial visits. The calculations of absolute changes in health outcomes were therefore based on this estimate. The health outcomes for patients incorrectly diagnosed as malaria were not estimated as it was assumed that they would be unchanged by the provision of a more effective drug. However, as both correctly and incorrectly diagnosed patients would be treated with antimalarials, all suspected cases were included in the cost calculations.

It is noteworthy that in their own documentation MSD report that they supply around 23 million antimalarial treatments per year, 50% to PHC facilities and 50% to hospitals[11]. This appears to be well in excess of the estimated 10mn outpatient diagnoses and estimated 283,000 inpatient admissions (scaled up for under-reporting) used in this report. It is not clear why this discrepancy arises, and particularly why such a large

share of MSD treatments go to hospitals, which are responsible for a relatively small share of cases according to the MTUHA. Although drug stock-outs are frequently reported, it is possible that there may be over-stocks in other facilities or areas of the country, which are then wasted. Further investigation to explore this discrepancy is essential in order to assess whether the current estimates are appropriate.

**Annex 2 Table 1.** Malaria outpatient and inpatient data for Tanzania, 1996

| | Under 5 years | Over 5 years | All ages |
|---|---|---|---|
| **Outpatient diagnoses of malaria** | | | |
| Health Centre & Dispensary | 1,832,764 | 2,769,157 | 4,601,921 |
| Hospital (excluding referral hospitals) | 127,752 | 162,406 | 290,158 |
| Total Outpatients | 1,960,516 | 2,931,563 | 4,892,079 |
| **Inpatient admission diagnoses of malaria** | | | |
| Total | 85,434 | 84,365 | 169,799 |

Source: Health Statistics Abstract, 1998, Ministry of Health, Tanzania(1)
Covers all government facilities and formal NGO and private facilities
Reporting Rates:
Annual Health Facility OPD – 51%
Annual District Inpatient – 60%

## Annex 3: Report on Health Seeking Behaviour and Antimalarial Treatment

Prepared for the Tanzanian Ministry of Health Task Force on Antimalarial Drug Policy

### Introduction:

Tanzania is in the process of revising its antimalarial treatment policy and health seeking behaviour is an important aspect to be considered in the development of this policy. Much work has been done in the field of care seeking and care seeking behaviours. However, this work is not compiled nor is it readily available to policy makers who need it. A one day workshop was organised to help in the compilation of this information. During the workshop an outline of the antimalarial treatment policy was presented by Dr. Abdulla (IHRDC), the experience of care seeking behaviours was presented by Dr. Mayombana (IHRDC & TEHIP), care seeking history for individuals who have died from acute febrile illness (malaria) was presented by Mr. Masanja (AMMP & TEHIP). Lastly, Dr Nsimba presented the sources and use of antimalarial for mothers with under five children in Kibaha area. The presentations were followed by discussions which identified important findings from all this research and gave recommendations of issues that require further research in order to assist the development of the antimalarial treatment policy for Tanzania. This paper summarises the presentations, discussions and recommendations.

### Antimalarial treatment policy framework

The goal of the antimalarial treatment policy is to use efficiently the available scarce resources to promote correct use and make available quality, efficacious antimalarials with acceptable safety at a price that both the individual and the community can afford. Hence, issues of the efficacy, safety, costs, access, quality of the products used etc. need to be considered. Furthermore, correct use and compliance to the recommended treatment are important parameters hence the contribution of treatment and care seeking behaviour. Health seeking behaviour studies also contribute information on the utilization and choice of health services by special affected groups like pregnant women and young children at different types and levels of care i.e. public/private, home/hospital, modern/traditional etc.. Issues of choice of health care providers and care seeking pattern for complicated malaria are highlighted e.g. the preference of traditional medicine for convulsions. Lastly, care seeking for treatment failures and side effects from the antimalarials drugs that are used may help in the selection of an appropriate antimalarial to be recommended in the policy.

### Household health seeking behaviour for malaria treatment

Studies continuing in Morogoro rural and Rufiji have showed that the biomedical model of malaria is restricted to uncomplicated malaria which is locally termed as ”homa”. Its treatment most often begins at home either with modern remedies such as antimalarials (chloroquine), antipyretics (panadol or Asprin) or

with traditional remedies.

Complicated malaria on the other hand is given quite different aetiology and treatment options. Cerebral malaria is mostly treated by traditional remedies. People believe that if a child with such a condition is taken to hospital it will most often result in a fatal outcome. Children are observed to wear fetishes (azma, hirizi) around their necks, wrists and waist as a protective mechanism against such illness that are characterised by fever and convulsions (degedege). Traditional healers end up treating most of the complicated malaria, therefore they have to be considered in the malaria case management effort.

It has been observed that information flows very slowly from the formal health sector to the household level where the decisions are made for treatment seeking. It takes a long time for people to get the information or understand that the formal health services can cater for complicated malaria or that changes/improvements have been made in the quality and quantity of services available at health facilities (e.g. IMCI). Poor communication channels between the health sector and the household are one of the problems. Should changes be made in the treatment policy then appropriate communication channels have to be developed and utilised.

Lastly, the community perceives malaria as a multiple illness with a multiple health seeking behaviour pattern. There is a lot of shifting or exchange from the modern to traditional facilities. The revision of the antimalarial treatment policy offers an opportunity to incorporate peoples beliefs and the traditional healers in the treatment of both uncomplicated and complicated malaria.

**Health seeking behaviour for acute febrile illness**

Facility based heath statistics show that about 1/3 of all deaths of admitted patients are due to malaria. Community based data on the type of services ever used in the period leading to death from acute febrile illness from three AMMP areas (Dar es salaam, Hai and Morogoro rural:1992-1998) show that 80% in Dar and Hai ever used a formal health service. The estimate was 56% for Morogoro rural. The data also show that 46% of the cases in Morogoro opted for traditional healers and about 7% had no treatment at all. Lastly, 31% of the cases in Hai had self treatment. The figures were about 17 and 14% for Morogoro and Dar es salaam respectively. This shows that there is high proportion of individuals with febrile illness that attend the formal health facilities but still end up dying. Data on the place of death from acute febrile illness in same areas and time, show that 53% of Dar cases died at home and 42% died at hospital. In Hai 40% died at home and 56% died at a hospital. In Morogoro 87% died at home and only 10% died at hospital. Information for Morogoro rural from 1992-1995 on the contact with health facilities in the illness leading to death show

that 56% with malaria contact formal health facilities while 29% contact traditional facilities and 15% had no contact with either service.

These data shows that although a large percentage of individuals with febrile illness do attend the formal health services, still a good proportion of them end up dying at home. Moreover, the information indicates that formal health services are unable to treat effectively acute febrile illnesses. There are many explanations of this scenario. The problem may be the use of non efficacious drugs (i.e. chloroquine) or that the patients attend the health facilities too late.

**Sources, availability and use of antimalarials in households**

The majority of malaria episodes are first recognised and responded to at the household level, where decisions on whether, when and where to seek treatment are being made. This is influenced by traditional beliefs, access and quality of existing health facilities and the financial position of the family. Management of malaria at the household level is vital in the antimalarial treatment policy and the control of malaria in general. Information collected in Kibaha area show that chloroquine the first line antimalarial, is widely available from the drug stores and ordinary shops. In this area, other antimalarials like fansidar, metakelfin and quinine are also widely available. Almost all of the residents live within 6-10 Km of a health facility and 47% within 2 Km.. 89% of the households usually utilise the public health facilities. On the sources of antimalarials, 58% obtained the antimalarials from the drug stores, 19% from ordinary shops and only 11% from public health facilities. 12% of the households had stocked antimalarials at home. 85% of mothers missed drugs during their last visit to a public health facility and of these 94% bought drugs, 2% visited private health facilities and 4% returned home without any medication. Concerning knowledge of chloroquine dosage, 70% of the mothers knew the correct adult dose regimen, 4% stated an over dosage and 10% an under dosage. While for paediatric dose only 20% knew the correct dose and 29% did not have any clue to the dose.

In summary mothers' knowledge of paediatric dosing of chloroquine was very poor. A simple antimalarial dosing regimen for children will be very helpful in ensuring adequate malaria management at household level. There is a need for educational programmes targeting especially mothers and guardians of young children to promote proper malaria management at household level.

The knowledge and dispensing practices of drug stores and ordinary shop sellers is not adequate. Although many households were accessible (with reference to distance) to health facilities, the facilities lacked drugs and the drugs stores remained the main source of antimalarials. Therefore there is a need to train the sellers on the appropriate use of antimalarials.

**Summary of relevant collected facts**

1. The community have different interpretations for simple and complicated malaria
2. The first recognition of malaria and the decision making about what is to be done is at home
3. There is high febrile illness (malaria) mortality despite high chloroquine consumption
4. Home treatment is very common
5. Knowledge on correct paediatric dosage is a problem while adult dosage is appropriate
6. Both traditional healers and drug stores/ordinary shops play an important role in malaria treatment

**Summary of important gaps in knowledge**

1. Exact or appropriate definition of access to health services (e.g. including time factor)
2. Consumer confidence on chloroquine efficacy
3. What proportion of acute febrile illness deaths are due to malaria
4. Quantifying the home treatment i.e. its source of drugs, storage, dosage, source of instructions, prescription and perception of side effect
5. Knowledge, attitude and practice toward antimalarials
6. Knowledge, attitude and behaviour of school children towards Sulphadoxine-Pyrimethamine
7. Trends in malaria mortality over the years 1992-1998
8. Ways of integration of the formal and traditional practices
9. Community perception on the introduction on new antimalarials (i.e. needs and demands)

**List of Participants**

Dr. Mwita- MOH - NMCP

Dr. Mandike- MOH - NMCP

Mr. Shirima - MOH - HEU

Mr Kisoka - NIMR

Mr Makundi - NIMR

Dr. Mbuya -TEHIP

Dr. Mayombana - IHRDC/TEHIP

Dr. de Savigny -TEHIP

Mr. Massanja - AMMP

Dr. Nsimba- MUCHS

Prof. Massele - MUCHS

Ms. Ritha Njau -WHO-TZ

Ms. Mohammed - IHRDC

Dr. Abdulla -IHRDC

## Annex 4: The provider costs of treating malaria patients at Mlimba Health Centre

### Objectives

The study calculated the non-drug costs of treating outpatients and inpatients diagnosed with malaria at Mlimba Health Centre, where an investigation of in vivo drug efficacy took place. The aims were to provide estimates of the unit cost per outpatient (OP) and inpatient (IP) (excluding drug costs), and to explore the likelihood of treatment cost savings from the introduction of a more effective first line treatment for malaria.

### Methods

**Perspective:** A provider perspective was adopted, including only costs incurred by the government. Patient costs were assessed separately (see Annex 5).

**Time frame of analysis:** Cost data were based on resource use data from financial year 1997/8, valued at 1999 prices. Utilization figures were based on calendar year 1998 records

**Boundaries:** Only costs incurred at the Health Centre level were included, excluding costs incurred at the District level, such as supervision.

**Year of costs/currency:** Calculations are in 1999 Tsh (US$1 = 780 Tsh)

**Data Sources:** Data were collected from records at the Health Centre and District level, interviews with staff, observation of resources actually available at the Health Centre, and the Medical Stores Department price catalogue.

**Calculation of capital costs:** Capital items were defined as those with a useful life of one year or more. These included health centre buildings, patient beds, furniture, ambulance, and laboratory equipment such as microscopes and refrigerators. Annualised values of relevant capital items were calculated using the replacement price, expected useful life and the real discount rate. The real discount rate was calculated based on the current nominal interest rate (Bank of Tanzania Discount Rate, average for June 1999) of 12.2%, and the annual inflation rate (% change July 1998 to July 1999) of 7.6%, to give real discount rate of 4.3% *(Source: National Bureau of Statistics, Dar es Salaam*).

**Calculation of recurrent costs:** The recurrent cost components included in the estimation were staff salaries, drugs, laboratory consumables (such as chemical reagents, oils, slides, cotton wool etc.), syringes, needles, IV sets, bed sheets, lamps and cookers, kerosene, fuel for ambulance, stationery, other supplies, and maintenance. Staff time spent on malaria cases was included in the costs as an opportunity cost of time that would have been spent on alternative activities, such as attending to other patient health problems at the health centre. Staff time was costed on the basis of the full gross salary costs including benefits.

**Allocation of Costs:** To derive a unit cost per patient diagnosed with malaria, it was necessary to apportion the costs of running the Health Centre between "malaria" and other activities. Costs were allocated between five cost centres, namely OP (outpatients), IP (inpatients), MCH (maternal-child-health), Lab (laboratory) and Admin (administration). Building costs were allocated to the different cost centres on the basis of floor area. Staff time was allocated to the different cost centres on the basis of time spent on different activities (from HMIS records and additional assumptions to break down OP and MCH). IP consumables used solely for malaria cases were allocated directly to malaria IP, plus a share of other consumables. The costs of the Lab and Admin cost centres were then reapportioned to OP, IP and MCH. Admin costs were allocated equally between OP, IP and MCH. Lab costs were allocated on the basis of the proportion of lab tests for malaria diagnoses.

The total OP cost attributable to malaria was calculated as the sum of:

- the costs of the OP cost centre times the proportion of OP visits attributed to malaria
- the costs of the Lab cost centre times proportion of lab tests for malaria OP, and
- one third of costs of Admin cost centre

The unit cost per malaria OP was then calculated as malaria OP costs divided by the number of malaria OP visits in 1998.

The total IP cost attributable to suspected malaria was calculated as the sum of:

- the costs of the IP cost centre times the proportion of IP admissions attributed to malaria
- the costs of the Lab cost centre times the proportion of lab tests for malaria IP
- one third of the costs of the Admin cost centre

The unit cost per malaria IP was then calculated as malaria IP costs divided by the number of malaria IP admissions in 1998. (It might be more appropriate to allocate on the basis on the share of IP days, rather than admissions, as admissions for other causes may have a different average length of stay, but data on days had not been collected.)

It is recognized that many of the cases were diagnosed as "malaria" on a purely clinical basis, and there is therefore likely to have been substantial over-diagnosis, particularly of outpatients.

**Results**

In 1998 suspected malaria accounted for 7,540 OP visits at Mlimba Health Centre or 42% of all visits, and 1,943 or 54% of all IP admissions. The facility had 13 staff: 1 Medical Assistant in Charge, 2 Medical Assistants, 1 Nurse MCH, 1 Nurse Midwife and 1 other Nurse, 2 Assistant Nurses, 1 Assistant Lab Technician, 1 Cleaner, 1 Watchman, 1 Cook and 1 Driver. Annual staff salary costs were Tsh 8,6mn. The total building cost was estimated at Tsh 15mn with a 40 year expected useful life.

The total and unit cost of treating malaria outpatients are shown in Annex 4 Table 1, and of treating malaria inpatients in Annex 4 Table 2. For malaria outpatients the total annual cost was estimated at Tsh 2,4mn ($3,039) of which 92% were recurrent costs. The bulk of the costs were made up of staff (44%) and laboratory supplies (43%). The unit cost per malaria outpatient was Tsh 314 ($0.40). For malaria inpatients the total annual cost was estimated at Tsh 6,4mn ($8,160) of which 71% were recurrent costs. The bulk of the costs were made up of staff (29%), equipment (25%) and laboratory supplies (21%). The unit cost per malaria outpatient was Tsh 3,276 ($4.20). It should be noted that these costs do not include drugs.

**Discussion**

As well as being interested in the total unit cost, we are also interested in what costs would be saved if the number of OP visits or IP admissions were reduced by the use of a more effective first line drug. To do this we need to estimate what proportion of the unit costs would be saved if a visit or admission were averted and what proportion are "fixed" i.e. do not vary with the number of patients.

Analysis of OP and IP unit costs shows that in practice by far the majority are likely to be fixed. This would cover:

- all capital costs (equipment and buildings)
- all administration costs
- certain consumables such as thermometers and stethoscopes
- staff costs as it is probably that an extremely large drop in patient numbers would be required before the number of staff could be reduced, especially as the clinic is currently understaffed (13 staff members compared to 21 "required" by establishment list).

- in addition in view of the fact that the number of lab tests done is currently constrained by the supplies provided in the kits, reducing the number of patients might not reduce the number of tests done.

This implies that savings in non-drug costs due to a reduction in patient numbers are likely to be very limited indeed. It is possible that more of these costs would become variable in response to a very large change in patient numbers, but this is unlikely from a change in first line drug, which is expected to mainly affect return rates only, and not incidence of disease and therefore initial visits.

However it is important to note that a reduction in patient numbers could potentially significantly improve the quality of care for all remaining patients due to a reduction in the number of drug and lab supply stockouts, shorter waiting times, and less over-loaded staff. In addition a reduction in treatment failure rates would also significantly reduce costs to patients who would avoid any costs of making a return visit to the health centre, visiting the hospital or consulting any other providers (see Annex 5).

**Annex 4 Table 1.** Malaria outpatient costs at Mlimba Health Centre (excluding drug costs) 1999 Tsh

| | Annual costs of suspected malaria OP | | | Unit cost per suspected malaria OP visit | | |
|---|---|---|---|---|---|---|
| | **capital** | **recurrent** | **total** | **capital** | **recurrent** | **total** |
| Equipment | 44,002 | - | 44,002 | 5.84 | - | 5.84 |
| Buildings | 91,743 | - | 91,743 | 12.17 | - | 12.17 |
| Consumables | - | 5,589 | 5,589 | - | 0.74 | 0.74 |
| Manpower | - | 1,046,957 | 1,046,957 | - | 138.85 | 138.85 |
| Admin | 8,737 | 156,552 | 165,289 | 1.16 | 20.76 | 21.92 |
| Laboratory | 52,619 | 964,364 | 1,016,984 | 6.98 | 127.90 | 134.88 |
| **Total Tsh** | **197,102** | **2,173,462** | **2,370,564** | **Tsh 26** | **Tsh 288** | **Tsh 314** |
| **Total US$** | **$253** | **$2,786** | **$3,039** | **$0.03** | **$0.37** | **$0.40** |

**Annex 4 Table 2.** Malaria inpatient costs at Mlimba Health Centre (excluding drug costs) 1999 Tsh

| | Annual costs of suspected malaria IP | | | Unit cost per suspected malaria IP admission | | |
|---|---|---|---|---|---|---|
| | **capital** | **recurrent** | **total** | **capital** | **recurrent** | **total** |
| Equipment | 1,587,153 | - | 1,587,153 | 816.86 | - | 816.86 |
| Buildings | 188,033 | - | 188,033 | 96.77 | - | 96.77 |
| Consumables | - | 1,190,720 | 1,190,720 | - | 613 | 613 |
| Manpower | - | 1,827,227 | 1,827,227 | - | 940.42 | 940.42 |
| Admin | 11,396 | 204,185 | 215,581 | 5.87 | 105.09 | 110.95 |
| Laboratory | 70,168 | 1,285,985 | 1,356,153 | 36.11 | 661.86 | 697.97 |
| **Total Tsh** | **1,856,750** | **4,508,116** | **6,364,866** | **Tsh 956** | **Tsh 2,320** | **Tsh 3,276** |
| **Total US$** | **$2,380** | **$5,780** | **$8,160** | **$1.23** | **$2.97** | **$4.20** |

## Annex 5: Use of antimalarials and the costs of seeking care for presumptive malaria in children attending for care at Mlimba Health Centre

### Summary of findings

- The health centre is being used as a primary health facility for care of children with presumptive malaria
- Self medication is common and children are frequently given drugs stored at home or bought at shops.
- Most households who visit the health centre do not have any financial outlay for treatment during the episode (partly because fees are not charged at this level for children under five). However, these households represent a selected sub-sample; those who do not come to the government health centre may be more likely to spend.
- Of those who do spend, the majority of costs are incurred before the health centre visit and are mainly made up of shop-bought drugs.
- The non-financial costs (i.e. opportunity costs of time) of visiting the health centre are significant.
- More detailed investigation is required to generate information on potential household cost savings from use of a more efficacious antimalarial in both the public and private sectors.

### Introduction:

Malaria is a major public health problem in Tanzania. The problem is being compounded by the emergence and progression of parasite resistance to commonly used antimalarials in Tanzania. The Ifakara Health Research & Development Centre, together with its collaborators was commissioned to assess the costs of treating malaria at a rural health facility and get a description of patient costs for children attending for care with a presumptive diagnosis of malaria at Health Centre level. As part of this study, an investigation of the patterns of drug use by families and the associated costs of this drug use was also done. A short description of the study and its results is presented here.

### Methods:

A prospective study was carried out in children under six years of age with diagnosis of malaria who attended the Mlimba Health Centre between May and August 1999. Children were screened, consent asked, recruited and randomly allocated to receive either SP or Amodiaquine, either supervised or unsupervised. The children were then followed up for 14 days to determine the treatment response. The National sentinel site antimalarial monitoring procedures for recruitment and determining treatment response were used (WHO/MAL/96.1077[8] & EANMAT manual). Follow-up was on day 3, 7 and 14 for the supervised patients

and on day 14 at home for the unsupervised patients. A questionnaire asking about the use of antimalarials at home and the cost incurred for treatment at home or for seeking care at a health facility was used. The questionnaire was applied to the care taker/guardians at recruitment, for patients with presumptive diagnosis of malaria and at the end of the 14 days. The questionnaires were also applied to the care takers for children who had a presumptive diagnosis of malaria but did not fit the inclusion criteria of the efficacy study. Data was entered in Foxpro® and analysis done in Stata.

**Results:**

199 care takers with children with presumptive diagnosis of malaria were interviewed on the day they brought their children for care and 175 follow up interviews were done.

The guardians comprised of 92.6% biological mothers of the children and 7.4% other relations, most being grandmothers and aunts. 84.9% (169) of the guardians can be classified as literate. (Other studies in the same area have demonstrated that those with more than four years of formal education can read Swahili text.) The age of the guardian ranged from 16 – 69, with a median of 27 years, 81.4% were married and 16.6% reported to be single.

The children whose guardians were interviewed were between 6 months and approximately 6 years with a mean of two years. 47.7% (95) of them were males. 15% of these children had been sent to a formal health facility once in the two weeks prior the interview and recruitment in the study. 2.2% had more than one visit to the health facility and 82.8% had not been sent to a health facility in the two weeks prior to recruitment.

Most children (67.9%) live within half an hour from a shop, where over the counter drugs like antimalarials are available and only 15.1% live more than one hour from a shop. To get to the health centre 87.6% came on foot, 7.9% by bicycle and 4.5% by car/bus. For 50% of guardians it takes less than half an hour to get to the facility. Time spent at the health centre per episode is substantial with 70.6% spending more than 3 hours, 22.6 % between 2-3 hours and only 6.8% less than 2 hours. Furthermore, most guardians (92.7%) are unable to continue with their work on that day. Most guardians come alone (81.4%) and 18.6% came with an escort.

For the current illness that necessitated attendance at the Mlimba Health Centre and led to recruitment into the study, 5.9% of the children had already been sent to a government hospital, 1.6% to a private hospital, 27% had bought some drug at the drug shops. 37.5 % had utilised 'spare drugs' at home. Only 1.6% of the

guardians reported attendance to a traditional healer prior the episode and 3.2% reported use of traditional medicines at home.

The use of nets was also high in the study population with 79.4% (158) having one, and out of these 74.1% were in use in the month prior the interview. Net treatment is still low in this population with only 15.2% of the nets treated.

An assessment of the costs incurred by the guardians in seeking care for their children was also done, covering treatment seeking before recruitment for the current episode, costs on the day of recruitment and costs in the two weeks following recruitment. The overall costs were between 5 - 5000 Tsh for the period before recruitment and this was mainly to buy drugs, to buy food stuffs and nutritional supplements and consumable (other medical supplies e.g. syringe cotton wool etc). The costs on the day of recruitment were between 20 - 600 Tsh which were mainly food stuffs, transport and note books for recording illness and treatment histories at the facility. The costs for the two weeks after recruitment were much lower than before recruitment (20 - 1600 Tsh) and were mainly on drugs and consumables. Details of the costs are in Annex 5 Table 1.

Children who satisfied the inclusion criteria were enrolled in the efficacy study (in vivo) and randomly allocated to receive either Amodiaquine or SP. Those that did not, were given the standard treatment of the health centre. Therefore, 40.2% (80) of the children were given amodiaquine, 42.2% (84) SP, 13.1% (26) chloroquine, 1% (2) quinine and the rest were not given any antimalarial. Paracetamol or Aspirin was given to 98% (195) of the children.

The efficacy of the amodiaquine and SP was estimated during the period of the study. Amodiaquine had 16.3% (95%CI, 9.4 - 25.5) day 14 treatment failure and SP had 6.3% (95%CI, 2.1 - 14.2). Patients' costs for the 14 day follow up period for the children who had received Amodiaquine and SP treatment are given in Annex 5 Table 2. The average cost for patients receiving Amodiaquine was actually lower than for those receiving SP, despite the fact that treatment failure was lower with SP. However, the small numbers of patient interviewed make it difficult to draw reliable conclusions. Ideally these should be compared to costs for patients receiving chloroquine, the current first line therapy, but data are not available. It is also not possible to draw conclusions about the difference in costs between patients who failed and those who were cured, because of the small number of treatment failures (data not shown).

**Discussion:**

The data collected in this study contributes to the body of detailed information being collected at facility and community levels in the study area, on the determinants and dynamics of drug resistance, in order to inform rational antimalarial treatment policy formulation. This study was designed to give a description of the costs associated with seeking care for malaria at the health centre level. It is recognised that there are several limitations to getting a true assessment of the costs in such a setting. Issues ranging from the representativeness of patients who utilise this particular facility, to the actual services provided at the facility influence the cost estimates. The fact that the research was being conducted and the research team was at the facility, possibly improved services in amount and quality, and may have reduced the need to buy drugs or other medical supplies during this period. It may also have improved efficiency and hence reduced the time spent at the facility. Moreover, the use of more efficacious drugs for the treatment of identified episodes mean that the costs identified after treatment reflect more what will happen should a more efficacious drug be used as a policy. However, with all its limitations this study has provided some useful information.

It had been observed that most of the children with febrile illness come from near the facility and therefore the health centre serves more as a primary facility for this condition. In theory the Health Centre should receive patients referred from the primary facilities i.e. the dispensaries. Most children also live close to where antimalarials are easily available and self medication is also common whereby children were either given drugs stored at home or drugs bought at the shops.

The drug costs contributed the bulk of the costs for the period before recruitment, where an overall average of 102 Tsh were spent compared to 42 Tsh after recruitment. Overall, the data show that patients' costs were lower in the follow-up assessment than before recruitment. This is also the case for the proportion of guardians who had to pay something. These data indicate that, with appropriate diagnosis and treatment with an effective drug using the current health services structure, direct patient costs are small. Unfortunately data are not available on patient costs with a less efficacious drug such as chloroquine as first line. We would expect a change in drug to mainly affect costs after the Health Centre visit. It is possible that, if it became known that there was a better drug available at the Health Centre, people would come earlier, therefore saving themselves some of the pre-visit costs but this needs to be investigated. The data also emphasise the role of small drug shops and private vendors in malaria management. Further investigation is also required to determine how the sale of a more efficacious drug by the drug vendors will affect overall patient costs for malaria episodes. An investigation of the cost-savings realised with the use of a more efficacious drug would require first, enough cases of failures interviewed to distinguish between household costs for failures and

cures, and secondly data on the difference in average household costs with the use of specific antimalarial at home.

In this study, less than 36% of all guardians had to pay money during the course of the illness of their child but most of the guardians (over 92%) had their work interrupted during the illness. Furthermore, additional time is lost caring for the child at home or visiting alternative providers. Although not quantified in monetary terms in this study, this loss in productivity may be substantial. The use of an efficacious drug to treat the episodes will also reduce the number of those interruptions and hence contribute to costs savings for the family.

**Annex 5 Table 1:** Household costs of presumptive malaria episodes in children before the recruitment visit, during the recruitment visit and during the following two weeks

| | Costs before Recruitment | | | Costs after Recruitment | | | Costs at Recruitment | | |
|---|---|---|---|---|---|---|---|---|---|
| **Item** | paid (%) | cost range in Tsh | Avg[a] (Tsh) | paid (%) | Cost range in Tsh | Avg[a] (Tsh) | paid (%) | cost range in Tsh | Avg[a] (Tsh) |
| Doctor/healer | 6.5 | 20 – 1200 | 17 | 0 | 0 | 0 | 1.2 | 500 - 600 | 6 |
| Notes book | 2.6 | 50 – 80 | 1 | 7.5 | 50 – 80 | 4 | 1.2 | 50 - 80 | 1 |
| Lab tests | 1.1 | 70 – 500 | 3 | 1.2 | 50 – 80 | 1 | 0 | 0 | 0 |
| Drugs | 28.7 | 10 – 2000 | 102 | 3.5 | 10 – 200 | 3 | 6.3 | 20 - 1600 | 42 |
| Consumables* | 4.3 | 5 – 2300 | 30 | 0 | 0 | 0 | 2.9 | 300 - 500 | 13 |
| Transport ** | 1.1 | 200 – 1600 | 10 | 1.7 | 400 – 600 | 9 | 0.6 | 1600 | 9 |
| Food & other | 11.3 | 20 – 2000 | 30 | 8.6 | 20 – 400 | 11 | 2.3 | 40 - 250 | 3 |
| **Overall costs** | **35.7** | **5 – 5000** | **193** | **15.5** | **20 – 600** | **28** | **9.8** | **20 - 1600** | **74** |

**Annex 5 Table 2:** Household costs of presumptive malaria episodes in children during the following two weeks for children given Amodiaquine and SP

| | Costs for Amodiaquine patients | | | Costs for SP patients | | | Average costs for Amodiaquine + SP patients | | |
|---|---|---|---|---|---|---|---|---|---|
| **Item** | paid (%) | cost range in Tsh | Avg[a] (Tsh) | paid (%) | Cost range in Tsh | Avg[a] (Tsh) | paid (%) | cost range in Tsh | Avg[a] (Tsh) |
| Doctor/healer | 0 | 0 | 0 | 2.7 | 500 – 600 | 14.7 | 1.2 | 500 – 600 | 6.8 |
| Notes book | 3.5 | 50 – 80 | 2.4 | 0 | 0 | 0 | 1.9 | 50 – 80 | 1.3 |
| Lab tests | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Drugs | 5.8 | 100 – 1600 | 48.3 | 6.7 | 20 – 1000 | 30.9 | 6.2 | 20 – 1600 | 40.3 |
| Consumables* | 2.3 | 500 | 11.5 | 4.0 | 300 – 500 | 17.3 | 3.1 | 300 – 500 | 14.2 |
| Transport ** | 0 | 0 | 0 | 1.3 | 1600 | 21.3 | 0.6 | 1600 | 9.9 |
| Food & other | 3.5 | 40 – 200 | 3.2 | 2.7 | 50 – 250 | 4.1 | 3.1 | 40 – 250 | 3.6 |
| **Overall costs** | **8.1** | **100 – 1600** | **65.4** | **13.3** | **20 - 1600** | **88.3** | **10.5** | **20 - 1600** | **76.1** |

* Other medical supplies e.g. cotton wool, syringes etc

** Transport to reach the health facility

Avg.[a] Average for all the patients i.e. Overall cost per case

## REFERENCES


1. Ministry of Health (1998). *Health Statistics Abstract, Vol. 1 Morbidity and Mortality Data*. Dar es Salaam: Health Information and Research Section, Planning and Policy Department, Ministry of Health, United Republic of Tanzania.
2. Ministry of Health. *Standard Treatment Guidelines*. Dar es Salaam: Ministry of Health, United Republic of Tanzania,
3. Ministry of Health (1999). *Summary report of the Task Force on Antimalarial Drug Policy, July 23, 1999*. Dar es Salaam: Ministry of Health, United Republic of Tanzania, 1999.
4. Bloland PB, Kazembe PN, Oloo AJ, Himonga B, Barat LM, Ruebush TK (1998). Chloroquine in Africa: critical assessment and recommendations for monitoring and evaluating chloroquine therapy efficacy in sub-Saharan Africa. *Tropical Medicine and International Health*; 3(7): 543-552.
5. Trape JF, Pison G, Preziosi MP, et al (1998). Impact of chloroquine resistance on malaria mortality. *C. R. Acad. Sci. Paris, Sciences de la vie*; 321: 689-697.
6. Goodman C, Coleman P, Mills A (1998). *The cost-effectiveness of changing the first line drug: an analysis of the treatment of uncomplicated malaria at outpatient facilities in sub-Saharan Africa*. Harare: Draft Position Paper prepared for meeting on "Confronting the challenge of antimalarial drug resistance in Africa".
7. Goodman C, Coleman P, Mills A (2000). *Economic analysis of malaria control in sub-Saharan Africa*. Strategic Research Series. Geneva: Published by the Global Forum for Health Research. 1-185
8. WHO/CTD (1996). *Assessment of therapeutic efficacy of antimalarial drugs for uncomplicated falciparum malaria in areas with intense transmission*. Geneva: WHO/MAL/96.1077.
9. Snow RW, Mung'ala VO, Forster D, Marsh K (1994). The role of the district hospital in child survival on the Kenyan Coast. *African Journal of Health Sciences*; 1(2): 71-75.
10. Medical Stores Department. *Schedule of Fund Utilisation 1999/2000*. Dar es Salaam: 1999.
11. Medical Stores Department. *MSD distribution of malaria supplies*. Dar es Salaam: 1999.
12. Price Waterhouse Coopers (1998). *Report on the survey into the distribution of and acounting for medical supplies for the period 1 July 1996 to 31 December 1997*.
13. Abel-Smith B, Rawal P (1992). Can the poor afford "free" health services? A case study of Tanzania. *Health Policy and Planning*; 7(4): 329-341.
14. Alilio M, Tembele R (1994). *Kilombero District Health Support: Socio-cultural assessment for the Swiss Development Co-operation*. NIMR/Ifakara Centre and Norconsult Tanzania Limited.

15. Nsimba SED, Warsame M, Tomson G, Massele AY, Mbatiya ZA (1999). A household survey of source, availability and use of antimalarials in a rural area of Tanzania. *Drug Information Journal*; 33(4): 1025-1032.
16. Medical Stores Department. *Essential Drugs and Medical Supplies, July 1999*. Dar es Salaam: 1999.
17. Management Sciences for Health (1998). *International Drug Price Indicator Guide*. Boston: Management Sciences for Health and the World Bank.
18. Gilson L, Alilio M, Heggenhougen K (1994). Community satisfaction with primary health care services: an evaluation undertaken in the Morogoro region of Tanzania. *Soc Sci Med*; 39(6): 767-80.
19. Baume C, Macwan'gi M (1998). *Care-seeking for illnesses with fever or convulsions in Zambia, Final Report*. The BASICS Project, USAID.
20. Barat LM, Himonga B, Nkunika S, et al (1998). A systematic approach to the development of a rational malaria treatment policy in Zambia. *Tropical Medicine and International Health*; 3(7): 535-542.
21. Gilson LJ (1992). *Value for Money?: The Efficiency of Primary Health Units in Tanzania*. London School of Hygiene and Tropical Medicine, University of London: PhD Thesis.
22. Kirigia JM, Snow RW, Fox-Rushby J, Mills A (1998). The cost of treating paediatric malaria admissions and the potential impact of insecticide treated mosquito nets on hospital expenditure. *Tropical Medicine and International Health*; 3: 145-150.
23. Health Research for Action (HERA). *Health Care Financing in Tanzania: Costing study of health services. Final Report, Volume I, October 1999*. Laarstraat, Belgium: 1999.
24. Williams HA, Kachur SP, Nalwamba NC, Hightower A, Simoonga C, Mphande PC (1999). A community perspective on the efficacy of malaria treatment options for children in Lundazi District, Zambia. *Tropical Medicine and International Health*; 4(10): 641-652.
25. Gilson L, Adusei J, Arhin D, Hongoro C, Mujinja P, Sagoe K (1997). Should African governments contract out clinical health services to church providers? In: Bennett S, McPake, B. & Mills, A., ed. Private Health Providers in Developing Countries". London: Zed Press.
26. Phillips-Howard PA (1998). *Managing the introduction of new antimalarial drugs to Africa: theory and practice*. Harare: Draft Position Paper prepared for meeting on "Confronting the challenge of antimalarial drug resistance in Africa".
27. WHO (1996). *Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options*. Geneva: TDR/Gen/96.1.
28. Watkins W (1998). *Antifolate combination alternative to Fansidar (pyrimethamine-sulfadoxine)*. Harare: Draft Position Paper prepared for meeting on "Confronting the challenge of antimalarial drug resistance in Africa".

29. White N (1999). Antimalarial drug reisstance and combination chemotherapy. *Philosophical Transactions of the Royal Society of London*; B(354): 739-749.
30. Goodman CA, Coleman PG, Mills AJ (1999). Cost-effectiveness of malaria control in sub-Saharan Africa. *Lancet*; 354: 378-85.
31. Hill JA, Lake S, Meek SR, Mehra S, Standing H (1996). *Approaches to malaria control in Africa, Part I: analysis and opportunities for malaria control support in selected countries in Africa*. London/Liverpool Malaria Consortium.
32. Olivar M, Develoux M, Chegou Abari A, Loutan L (1991). Presumptive diagnosis of malaria results in a significant risk of mistreatment of children in urban Sahel. *Transactions of the Royal Society of Tropical Medicine and Hygiene*; 85(6): 729-30.
33. Stein CM, Gelfand M (1985). The clinical features and laboratory findings in acute *Plasmodium falciparum* malaria in Harare, Zimbabwe. *Central African Journal of Medicine*; 31(9): 166-70.
34. Guiguemde TR, Ouedraogo I, Ouedraogo JB, Coulibaly SO, Gbary AR (1997). Malaria morbidity in adults living in urban Burkina Faso. *Medecine Tropicale Marseilles*; 57(2): 165-8.
35. Brinkmann U, Brinkmann A (1991). Malaria and health in Africa: the present situation and epidemiological trends. *Tropical Medicine and Parasitology*; 42(3): 204-13.
36. Slutsker L, Chitsulo L, Macheso A, Steketee RW (1994). Treatment of malaria fever episodes among children in Malawi: results of a KAP survey. *Tropical Medicine and Parasitology*; 45(1): 61-4.
37. McCombie SC (1996). Treatment seeking for malaria - a review of recent research. *Social Science and Medicine*; 43(6): 933-945.
38. Watkins WM, Mosobo M (1993). Treatment of Plasmodium falciparum malaria with pyrimethamine-sulfadoxine: selective pressure for resistance is a function of long elimination half-life. *Transactions of the Royal Society of Tropical Medicine and Hygiene*; 87(1): 75-8.
39. White NJ, Olliaro PL (1996). Strategies for the prevention of antimalarial drug resistance: Rationale for combination chemotherapy for malaria. *Parasitology Today*; 12(10): 399-401.
40. Curtis CF, Otoo LN (1986). A simple model of the build-up of resistance to mixtures of anti-malarial drugs. *Transactions of the Royal Society of Tropical Medicine and Hygiene*; 80(6): 889-92.
41. Kachur SP, Adeniyi JD, Mwenesi H (1998). *Rational use of antimalarial drugs to slow the development of resistance: education and training for health care workers and the community*. Harare: Draft Position Paper prepared for meeting on "Confronting the challenge of antimalarial drug resistance in Africa".
42. White NJ (1992). Antimalarial drug resistance: the pace quickens. *Journal of Antimicrobial Chemotherapy*; 30(5): 571-85.

43. Steketee R, Macheso A, Heymann D, et al (1995). *A decade of progress in malaria policy and program development in Malawi: 1984-1993*. Washington DC: USAID.
44. Foster SD (1991). Pricing, distribution, and use of antimalarial drugs. *Bulletin of The World Health Organization*; 69(3): 349-363.