Cost-effectiveness of malaria control in sub-Saharan Africa

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Summary

Background Information on the cost-effectiveness of malaria control is needed for the WHO Roll Back Malaria campaign, but is sparse. We used mathematical models to calculate cost-effectiveness ratios for the main prevention and treatment interventions in sub-Saharan Africa.

Methods We analysed interventions to prevent malaria in childhood (insecticide-treated nets, residual spraying of houses, and chemoprophylaxis) and pregnancy (chloroquine chemoprophylaxis and sulfadoxine-pyrimethamine intermittent treatment), and to improve malaria treatment (improved compliance, improved availability of second-line and third-line drugs, and changes in first-line drug). We developed models that included probabilistic sensitivity analysis to calculate ranges for the cost per disability-adjusted life year (DALY) averted for each intervention in three economic strata. Data were obtained from published and unpublished sources, and consultations with researchers and programme managers.

Findings In a very-low-income country, for insecticide treatment of existing nets, the cost-effectiveness range was US$4–10 per DALY averted; for provision of nets and insecticide treatment $19–85; for residual spraying (two rounds per year) $32–58; for chemoprophylaxis for children $3–12 (assuming an existing delivery system); for intermittent treatment of pregnant women $4–29; and for improvement in case management $1–8. Although some interventions are inexpensive, achieving high coverage with an intervention to prevent childhood malaria would use a high proportion of current health-care expenditure.

Interpretation Cost-effective interventions are available. A package of interventions to decrease the bulk of the malaria burden is not, however, affordable in very-low-income countries. Coverage of the most vulnerable groups in Africa will require substantial assistance from external donors.

Lancet 1999; **354:** 378–85

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Introduction

One of the main initiatives of Gro Harlem Brundtland, the new Director General of WHO, was to launch the Roll Back Malaria campaign, which aims to generate a substantial expansion in effective malaria prevention and treatment.[1,2] The initial focus is on sub-Saharan Africa, where malaria is the most important infectious disease in childhood. Policy makers need information on the costs and effectiveness of interventions. The existing knowledge base on cost-effectiveness is, however, sparse, and is limited to a few studies that are hard to compare, generalise, or relate to operational situations. Although more studies are required, results will not be available to inform urgent decisions on resource allocation.

To address this gap in available data, we estimated cost-effectiveness ratios for the main prevention and treatment interventions in sub-Saharan Africa. We used an innovative modelling approach based on probabilistic sensitivity analysis, which we believe provides policy makers with robust conclusions, despite the imperfect data available.

Methods

Models

Our analyses were restricted by the availability of cost and effectiveness data to a subset of interventions to prevent malaria in childhood (insecticide-treated nets, residual spraying of houses, and chemoprophylaxis); to prevent malaria in pregnancy (chloroquine chemoprophylaxis and sulfadoxine-pyrimethamine intermittent treatment); and to improve the treatment of uncomplicated malaria (better compliance with drugs, improved availability of second-line and third-line drugs, and changes in first-line drug treatment).

We obtained cost data through reviews of published and unpublished literature, programme budgets, price catalogues, and consultation with researchers and programme managers. Costs were defined as incremental direct costs to the provider and to the community, and were calculated by the ingredients approach.[3] We converted capital costs into annualised values using a discount rate of 3%, and all costs were expressed in 1995 US$. Salary costs were estimated for each of three economic strata. The strata were defined based on gross national product per person, as very low income (<$315), middle income ($315–1000), and higher income (>$1000). We used a single price for other inputs, such as drugs and insecticide, since most are traded internationally.

We modelled the effectiveness of each intervention based on a hypothetical population derived from a west African life table, with a life expectancy at birth of 50 years for very-low-income and middle-income countries, and a general pattern life table, with a life expectancy at birth of 65 years for higher-income countries.[4] Effectiveness was calculated in terms of disability-adjusted life years (DALYs) averted, a measure of health outcome incorporating premature death and morbidity or disability. DALYs were calculated from the age-specific life expectancies taken from the appropriate life tables, and information on the duration of morbidity or disability, and disability weights given to each disorder in the Global Burden of Disease study.[5] We discounted DALYs at 3%, but did not

Model variables	Probability distribution	Distribution parameters
Baseline estimates used in model of morbidity and mortality for children younger than 5 years		
Annual incidence of clinical episodes of malaria	Triangular	Mode 1·5 Minimum 1·0 Maximum 2·9
Percentage of episodes that are severe	Triangular	Mode 5% Minimum 3% Maximum 7%
Percentage of severe cases that result in neurological sequelae	Triangular	Mode 1·32% Minimum 0·41% Maximum 2·24%
Prevalence of malaria-associated anaemia	Point estimate	9%
Insecticide-treated nets		
Decrease in all-cause mortality in children aged 1–59 months*	Normal	Mean 19% (95% CI 14–24)
Decrease in malaria-related morbidity in children aged 1–59 months*	Normal	Mean 46% (95% CI 41–51)
Net re-treatment rate	Triangular	Mode 30% Minimum 20% Maximum 80%
Percentage of children sleeping under net	Triangular	Mode 72% Minimum 50% Maximum 97%
Cost per child younger than 5 years/year in very-low-income country		
Insecticide treatment only	90% range	$0·37–1·70
Nets and insecticide treatment	90% range	$3·35–10·98
Residual spraying		
Decrease in all-cause mortality in children aged 0–11 months	Triangular	Mode 52% Minimum 41% Maximum 59%
Compliance (% of households allowing houses to be sprayed)	Triangular	Mode 83% Minimum 70% Maximum 95%
Cost per child younger than 5 years/year in very-low-income country		
One spraying round/year	90% range	$5·76–10·18
Two spraying rounds/year	90% range	$11·53–20·36
Chemoprophylaxis for children		
Decrease in all-cause mortality in children aged 6–59 months	Normal distribution truncated at 95% CI	Mean 49% (95% CI 2–74)
Decrease in malaria-related morbidity in children aged 6–59 months	Normal distribution truncated at 95% CI	Mean 73% (95% CI 25–90)
Compliance	Uniform	Minimum 29% Maximum 72%
Cost per child aged 6–59 months/year in very-low-income country		
With existing VHW network, perennial transmission	90% range	$1·61–2·73
Including cost of VHW network, perennial transmission	90% range	$5·34–9·54

VHW=village health workers. *Data on decreases in mortality with insecticide-treated nets are based on results of meta-analysis for five trials that included mortality as an outcome.[9] CI for decreases in morbidity and mortality are slightly underestimated since they are not adjusted for group randomisation. Adjustment of CI would not change significance of effectiveness estimates (C Lengeler, personal communication). Costs were adjusted for non-compliance. All costs in 1995 US$.

Table 1: **Selected model variables for prevention in childhood**

weight them for age because the impact of the age-weighting function used in the Global Burden of Disease study is controversial.[6]

We obtained data on effectiveness from randomised controlled trials where possible, but adjusted them to estimate operational effectiveness with compliance rates recorded in more realistic settings. We adjusted effectiveness estimates for insecticide-treated nets by realistic net re-treatment rates and the proportion of children correctly using nets; for spraying, to allow for refusal by some households; for chemoprophylaxis for children and case management by realistic estimates of compliance with therapy; and for drug regimens during pregnancy by compliance and the probability of attending antenatal care. In the absence of better evidence, we assumed a linear relation between compliance and effectiveness in each case, such that zero compliance resulted in zero effectiveness, and the degree of compliance achieved in the trial resulted in the trial decreases in mortality and morbidity.

We combined DALYs averted with costs to produce a likely range for the cost per DALY averted of each intervention. To allow for the high degree of uncertainty and variability surrounding many of the variables, we assigned probability distributions to the model inputs.[7] If only range information was known for a variable, a uniform distribution was assigned; if available data showed a peaked distribution, a triangular distribution was used; and if data on the mean value and CI were available, for example from clinical trials, we constructed a normal distribution. The models were iterated according to Monte Carlo simulations, with Palisade @RISK software (version 3.5), and the cost-effectiveness-ratio output was expressed as a probability distribution rather than as a single point estimate. We calculated the mean and range in which 90% of the cost-effectiveness ratios fell, termed the cost-effectiveness range, as summary indicators. From guidelines provided for countries with gross national product per person of less than $765, we classified an intervention as highly attractive if the cost-effectiveness range was entirely less than $25, and attractive if it was entirely less than $150.[8]

Preventive interventions

For insecticide-treated nets, residual spraying, and chemoprophylaxis for children, we used a model to explore their cost-effectiveness in decreasing morbidity and mortality in children younger than 5 years. We assumed that effectiveness was the same in areas of seasonal and perennial transmission since the relation between length of transmission season and effectiveness is not well understood. Annual cost estimates were adjusted by season length, for example, to account for months of chemoprophylaxis required per year.

The analysis of insecticide-treated nets assumed annual communal treatment of nets with the insecticide deltamethrin, which lasts for 1 year with limited washing. We drew estimates of the effectiveness of insecticide-treated nets from the Cochrane meta-analysis of WHO/TDR trials in sub-Saharan Africa.[9] We used two possible scenarios: nets were distributed to households as part of the programme and were treated (insecticide treatment and nets), and insecticide treatment was provided for nets already owned by households (insecticide treatment only). We assumed that effectiveness was the same in the two scenarios, but costs were higher in the first scenario because of the inclusion of an annualised net cost.

Model variables	Probability distribution	Distribution parameters
Mean birthweight in unprotected primigravidae	Truncated Normal	Mean 2·78 kg (SD 0·082)
SD of birthweight in unprotected primigravidae	Truncated Normal	Mean 0·47 kg (SD 0·098)
Increase in birthweight after chemoprophylaxis or intermittent treatment	Truncated Normal	Mean 0·101 kg (SD 0·042)
Compliance to prescribed drug		
Chloroquine (average for whole course)	Uniform	Minimum 25% Maximum 57%
Sulfadoxine-pyrimethamine (per dose)	Uniform	Minimum 85% Maximum 95%
Cost per primigravidae for each pregnancy in very-low-income country		
Chloroquine chemoprophylaxis	90% range	$1·02–2·08
Sulfadoxine-pyrimethamine intermittent treatment	90% range	$0·86–1·90

Costs adjusted for non-compliance. All costs in 1995 US$.

Table 2: **Selected model variables for prevention in pregnancy**

Residual spraying calculations were based on a government-run programme that used the insecticide λ-cyhalothrin, which lasts 3–6 months. In the absence of up to date evidence on the health impact of residual spraying, we relied on decreases in infant mortality recorded in three controlled trials in the 1950s and 1960s.[10] No health effects outside this age-group or any decrease in morbidity could be included.

Chemoprophylaxis for children consisted of distribution of pyrimethamine and dapsone (Maloprim) every 2 weeks to children aged 6–59 months by village health workers. We based the analysis on two scenarios: villages with existing networks of village health workers, and villages in which networks of village health workers had to be established to run chemoprophylaxis programmes. We based the estimate of effectiveness on a trial in The Gambia[11] and calculated costs for seasonal (6 months) and perennial transmission. Key model variables for the interventions to prevent malaria in childhood are shown in table 1.

The interventions to prevent malaria in pregnancy consisted of two drug regimens for primigravidae only: weekly chloroquine chemoprophylaxis or two intermittent treatments with sulfadoxine-pyrimethamine. We based the estimate of effectiveness on the Cochrane meta-analysis of chemoprophylaxis,[12] which showed a significant increase in the birthweight of babies born to primigravidae (but not multigravidae). Although no study included in the meta-analysis used the sulfadoxine-pyrimethamine regimen, we assumed that a similar effect on birthweight would be found, since this regimen is effective in decreasing the prevalence of placental parasitaemia and severe maternal anaemia.[13,14] The sample sizes of the studies in the meta-analysis were too small to show a significant effect on neonatal mortality, and, therefore, we modelled the impact. We constructed an initial-birthweight distribution from empirical estimates, and estimated birthweight-specific neonatal mortality rates based on African data.[15,16] The impact of a shift in the birthweight distribution on the neonatal mortality rate was calculated and converted to DALYs averted. Costs assumed the addition of the intervention to an existing antenatal care programme. Key model variables are shown in table 2. We assessed the interventions at various rates of RII/RIII parasitological resistance[17] to chloroquine and sulfadoxine-pyrimethamine. We assumed that parasitological cure was required to increase birthweight.[18] We restricted the analysis of all preventive interventions to areas of moderate to high malaria transmission, since effectiveness data were unavailable for low-transmission or epidemic areas.

Interventions to improve treatment

Few assessments of interventions to improve treatment include evidence on health outcomes. We therefore developed a decision-tree model based on patients presenting at an outpatient facility with suspected uncomplicated malaria, incorporating probabilities of treatment failure, developing severe malaria, and seeking health care. We based estimates for the probabilities on published and unpublished data and, if data were unavailable, relied on discussion with expert researchers and clinicians. We used the model to translate changes in intermediate outcomes, such as compliance and drug efficacy, to the final health outcomes of full recovery, death, or survival with neurological sequelae. The impact of an intervention to improve treatment was modelled as a change in one or more of the probabilities in the decision tree. Effectiveness was estimated for two broad epidemiological strata of low and high transmission, based on differences in the age distribution of presenting cases, the accuracy of clinical diagnosis, and the probability of developing severe malaria. We assessed interventions at various rates of clinical failure with chloroquine.

Model variables	Probability distribution	Distribution parameters
Average age of death due to malaria		
High transmission age <5 years	Point estimate	1·2 years
High transmission age >5 years	Point estimate	20 years
Low transmission age <5 years	Point estimate	2 years
Low transmission age >5 years	Point estimate	30 years
Proportion of cases age <5 years		
High transmission	Point estimate	0·5
Low transmission	Point estimate	0·2
Compliance		
Chloroquine	Uniform	Minimum 20% Maximum 50%
Sulfadoxine-pyrimethamine	Uniform	Minimum 85% Maximum 95%
Oral quinine	Uniform	Minimum 10% Maximum 25%
Amodiaquine	Uniform	Minimum 30% Maximum 60%
Adequate clinical response rate		
Chloroquine	(Varied)	
Sulfadoxine-pyrimethamine	Triangular	Mode 93% Minimum 63% Maximum 99%
Oral quinine	Uniform	Minimum 99·5% Maximum 100·0%
Amodiaquine	Triangular	Mode 85% Minimum 80% Maximum 90%
True prevalence of malaria among suspected outpatient cases		
High transmission	Uniform	Minimum 35% Maximum 58%
Low transmission	Uniform	Minimum 10% Maximum 20%
Develop severe malaria after failing first-line drug		
High transmission age <5 years and low transmission all ages	Triangular	Mode 5% Minimum 3% Maximum 7%
High transmission age >5 years	Triangular	Mode 1% Minimum 0·5% Maximum 1·5%
Probability of seeking care at formal facility	Uniform	Minimum 19% Maximum 88%
Drug costs (per person age >5 years for each treatment)		
Chloroquine	Triangular	Mode $0·13 Minimum $0·10 Maximum $0·16
Sulfadoxine-pyrimathamine	Triangular	Mode $0·14 Minimum $0·12 Maximum $0·15
Oral quinine	Triangular	Mode $0·20 Minimum $0·18 Maximum $0·21
Amodiaquine	Triangular	Mode $2·68 Minimum $2·36 Maximum $3·15
Prepackaging, training, and health education to improve compliance		
Increase in compliance	Triangular	Mode 20% Minimum 10% Maximum 30%
Incremental cost/case treated	Uniform	Minimum $0·05 Maximum $0·15

Costs adjusted for non-compliance. All costs in 1995 US$.

Table 3: **Selected model variables for improvement in case management**

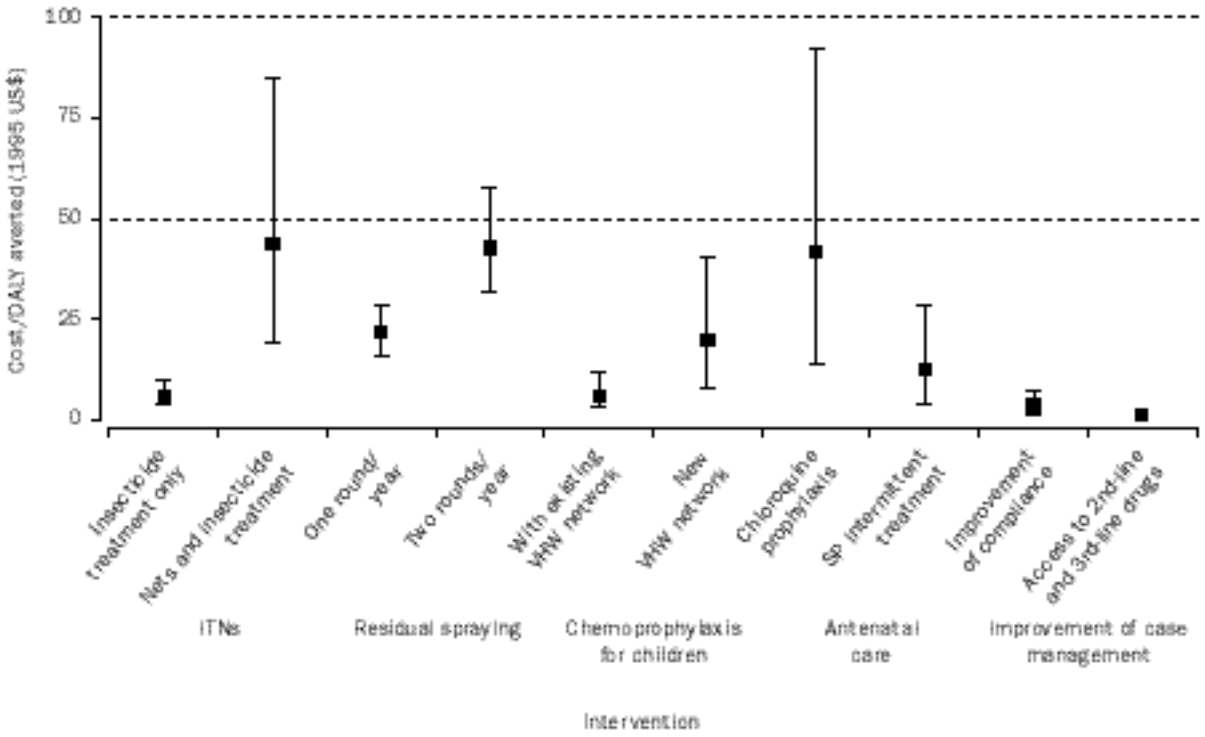

Figure 1: **Cost-effectiveness ranges and means in a very-low-income country with high transmission**
Mean and cost-effectiveness range. VHW=village health worker; SP=sulfadoxine-pyrimethamine; ITN=insecticide-treated nets—one treatment with deltamethrin per year, no insecticide resistance; residual spraying=λ-cyhalothrin, no insecticide resistance; chemoprophylaxis for children=pyrimethanine and dapsone, perennial transmission, no resistance to pyrimethamine and dapsone; antenatal care=primigravidae only, 50% chloroquine RII/RIII resistance, 10% sulfadoxine-pyrimethamine RII/RIII resistance; improvement in case management=chloroquine as first-line drug with 30% clinical failure.

We modelled three interventions: improvement of chloroquine compliance through training of providers, education of patients and carers, and prepackaging of chloroquine in plastic bags;[19,20] increased availability of second-line and third-line drugs (sulfadoxine-pyrimethamine and quinine) at peripheral facilities for patients experiencing treatment failure with chloroquine;[21] and changing the first-line drug for uncomplicated malaria[22] from regimen one, in which chloroquine is the first-line drug, sulfadoxine-pyrimethamine the second-line drug, and quinine the third-line drug, to regimen two, in which sulfadoxine-pyrimethamine is the first-line drug, amodiaquine the second-line drug, and quinine the third-line drug. The incremental costs for this and the second intervention comprised any increase in the costs of new drugs used, as well as expenses associated with changes in treatment guidelines.[23] Key variables for the case-management model are shown in table 3.

Results

The main cost-effectiveness results for a very-low-income country with high transmission showed that all interventions assessed would be an attractive use of resources according to the guidelines,[8] since the cost-effectiveness range was less than $150 in each case. A subset of the interventions was always lower than $25 and would, therefore, be classified as highly attractive (figure 1).

The cost-effectiveness of insecticide-treated nets is dependent on whether it is necessary to distribute nets. If so, the cost-effectiveness range in a very-low-income country was $19–85. If only insecticide treatment were required, the range would be decreased to $4–10. If two treatments were required per year, for instance because of the use of an insecticide with a 6-month duration, the range increased to $25–96 for insecticide treatment and nets, and $9–23 for insecticide treatment only.

The cost-effectiveness of residual spraying depended on the number of spraying rounds required per year. For one round per year, the cost-effectiveness range in a very-low-income country was $16–29, and doubled to $32–58 for two rounds per year. If slightly cheaper insecticides were used, the range was slightly lower, but the difference marginal.

The cost-effectiveness of chemoprophylaxis for children depended on whether a network of village health workers already existed. With an existing network, the cost-effectiveness range in very-low-income countries with perennial transmission was $3–12. If a new network had to be established, the range increased to $8–41. For seasonal transmission, costs were lower and the results more favourable, with a range of $2–7 with existing village health workers and $7–36 with establishment of a new network.

The results for these three interventions assumed zero resistance to insecticide and pyrimethamine and dapsone. Since resistance to chloroquine and sulfadoxine-pyrimethamine is widespread, we have represented the results for interventions to prevent malaria in pregnancy and improve treatment at realistic rates of drug resistance[24] (figure 1). For antenatal chloroquine chemoprophylaxis with 50% RII/RIII chloroquine parasitological resistance, the cost-effectiveness range was $14–93. For sulfadoxine-pyrimethamine intermittent treatment with 10% RII/RIII resistance, the cost-effectiveness range was $4–29. The chloroquine regimen was less cost-effective than the sulfadoxine-pyrimethamine regimen, even when resistance was the same for both drugs, because the sulfadoxine-pyrimethamine regimen was cheaper[25] and was assumed to have higher compliance because it involved only two doses, compared with weekly doses of

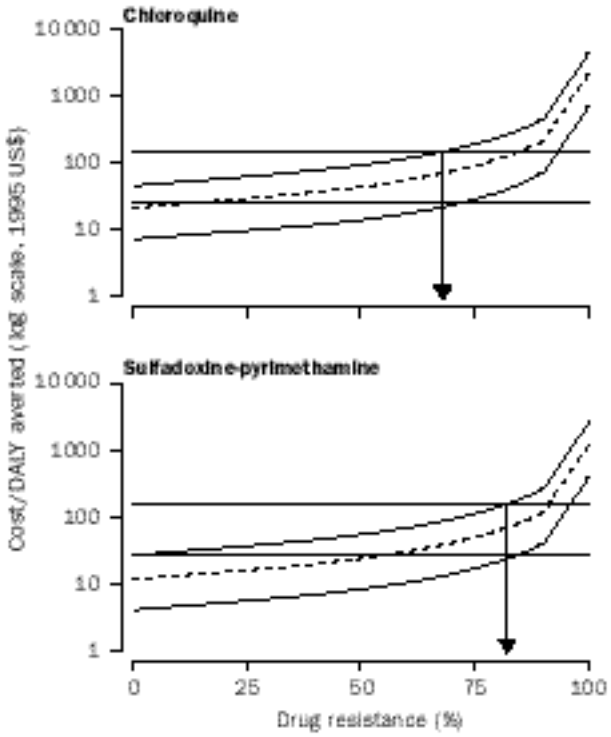

Figure 2: **Mean and cost-effectiveness range for chloroquine chemoprophylaxis and sulfadoxine-pyrimethamine intermittent treatment, as a function of RII/RIII drug resistance, for very-low-income countries**

Horizontal lines show $150 (top) and $25 (bottom); arrow shows rate of RII/RIII resistance above which cost-effectiveness range is no longer entirely lower than $150.

chloroquine. The cost-effectiveness range for the sulfadoxine-pyrimethamine regimen remained lower than $150 if coverage were extended to all gravidae (assuming zero effectiveness for multigravidae), or if three, rather than two, treatments were provided per pregnancy. The relation between the cost-effectiveness range and degree of drug resistance for very-low-income countries is shown for the two regimens in figure 2. The cost-effectiveness range for the chloroquine regimen remained lower than $150 up to 69% RII/RIII resistance, and the sulfadoxine-pyrimethamine regimen up to 83% resistance.

For the interventions to improve case management, the rate of clinical rather than parasitological failure was most relevant to the analysis. Results are shown for a chloroquine clinical failure rate of 30% (figure 1). Improvement of compliance through training, health education, and prepackaging was cost-effective: for a very-low-income country with high transmission the cost-effectiveness range was $2–8. The range remained less than $25 for all degrees of chloroquine resistance lower than 77%. In low-transmission areas, the cost-effectiveness range was lower than $25 up to 24% resistance, and lower than $150 up to 87% resistance.

Improvement of the availability of second-line and third-line drugs was similarly cost-effective. For a very-low-income country with high transmission, the cost-effectiveness range was $0·7–3·0. As chloroquine resistance increased, the intervention became more cost-effective, since it is even more important to have alternative drugs available. The cost-effectiveness range was lower than $25 at any degree of resistance in areas of high transmission, and at any degree of resistance higher than 6% in areas of low transmission. Improvement of compliance and of drug availability were less cost-effective in areas of low transmission because the true prevalence of malaria among suspected cases was assumed to be lower,[26] which would mean that the benefits of the intervention were experienced by a smaller proportion of patients.

A switch from chloroquine to single-dose sulfadoxine-pyrimethamine as first-line drug seemed cost-effective at any degree of chloroquine resistance in areas of high or

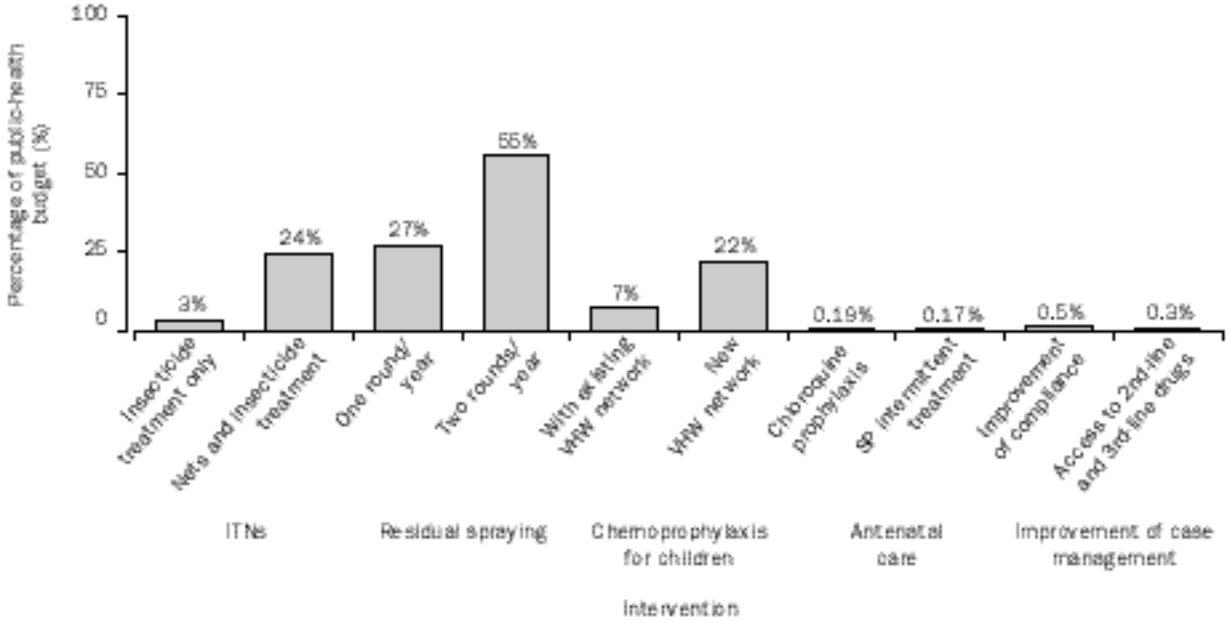

Figure 3: **Total cost of full coverage of target population as a percentage of a typical public-sector health care budget in a very-low-income country**

Based on Tanzanian population[27] and health-sector budget data[28] (combined donor and government funds). Assumes no cost recovery. VHW=village health worker; SP-sulfadoxine-pyrimethamine; ITN=insecticide-treated nets—one treatment of deltamethrin a year; residual spraying=λ-cyhalothrin; chemoprophylaxis for children=pyrimethamine and dapsone, perennial transmission; antenatal care=primigravidae only; improvement of case management=chloroquine as first-line drug.

low transmission because compliance was assumed to be much higher with sulfadoxine-pyrimethamine than with the 3-day chloroquine regimen, and the cost of treatment similar for the two drugs.[25] The additional costs of the replacement second-line drug and revision of the treatment guidelines therefore seemed to be good value relative to the benefits of the increased cure rate. This static analysis does not take into account, however, the central concerns that resistance to sulfadoxine-pyrimethamine will rapidly increase if it is widely adopted, and that affordable alternative antimalarials will not be available. Analytical methods must allow for the growth of drug resistance over time, and incorporate trade-offs between higher drug costs, immediate decreases in morbidity and mortality, and potential increases in resistance to replacement drugs that could lead to higher morbidity and mortality in the future. We could not, therefore, summarise this intervention in a single cost-effectiveness ratio, and it is excluded from figure 1.

To explore the trade-offs involved in changing the first-line drug, the case-management model was extended to cover 10 years, and drug resistance was allowed to grow over time. The model will be presented in detail elsewhere. The conclusions drawn from this model were strikingly different. For example, with a starting chloroquine clinical failure rate of 20%, the optimum time to switch to sulfadoxine-pyrimethamine could be delayed for several years, which would lead to higher rates of mortality in the short to medium term. The optimum time to change drugs according to effectiveness or cost-effectiveness criteria was dependent on empirical factors, such as the initial degree and growth rates of resistance, and subjective factors relating to the time preferences of policy makers, and their attitude to risk.

Cost-effectiveness ratios for middle-income countries were similar to those for very-low-income countries; the relative cost-effectiveness of the interventions was unchanged, and the cost-effectiveness ranges in each case were only slightly higher. For all interventions, the cost-effectiveness ranges were entirely lower than $150. In higher-income countries, the cost-effectiveness ranges were notably higher for all of the prevention interventions, but similar for the interventions to improve case management. The cost-effectiveness ranges for prevention increased partly because of higher costs for non-traded goods, and partly because of the lower underlying mortality rates, which meant that fewer DALYs were averted for a given proportionate decrease in morbidity or mortality.

The estimated total cost of full coverage of the interventions as a percentage of the existing public-sector health budget for a typical very-low-income country is shown in figure 3 (based on Tanzanian population and health-sector budget data[27,28]).

Discussion

The modelling approach enables results to be extrapolated from trials to operational settings, and the standardised analytical framework facilitates comparison of the cost-effectiveness of different malaria control interventions. The representation of the results as realistic ranges rather than simple point estimates incorporates much of the uncertainty surrounding the input parameters, and allows robust conclusions to be drawn from uncertain data. Nonetheless, although we stratified our results by economic and epidemiological zones where possible, substantial generalisation across areas was necessary, because of the lack of data.

Although the approach we used was common to all assessments, some variation in methods was required to accommodate the constraints of data availability. For example, information on the health outcomes of spraying was restricted to old infant mortality data, but for insecticide-treated nets, up-to-date morbidity and mortality data were available for all children aged 1–59 months. As an alternative approach, we proxied spraying effectiveness with the results of the meta-analysis of insecticide-treated nets,[9] since similar parasitological results have been achieved with the two interventions.[29] With this approach, the cost-effectiveness range for spraying in a very-low-income country was increased slightly, at $18–36 for one round per year, and $36–72 for two rounds per year, but this made no difference to the overall conclusions.

Data on other interventions are also imperfect and highlight key weaknesses in the research evidence available to support the Roll Back Malaria campaign. The effectiveness and costs of chemoprophylaxis for children were derived from a single study, and few trials of treatment interventions are available. The results of the analyses of antenatal prevention and interventions to improve treatment are dependent on extrapolation of intermediate outcomes (eg, birthweight, compliance, and efficacy) to final health outcomes. The lack of data precluded analysis of several potentially important interventions, including environmental management, epidemic surveillance and prevention, and interventions to improve the treatment of severe malaria.

Cost-effectiveness depends on various factors specific to each intervention, but certain common influences can be identified. These include the length of the transmission season (through the effect on costs), the price of key commodities (such as nets and drugs), behavioural factors (such as compliance with drug regimens and re-treatment rates for nets), the degree of existing infrastructure, and the degree of drug resistance. Because there is substantial regional variation in these factors, analyses should be adapted at a local level to guide country policy.

In particular, incremental costs, and therefore, cost-effectiveness, are affected by the degree of existing infrastructure. The proportion of people who own nets affects the cost-effectiveness of insecticide-treated nets, the existence of a network of village health workers affects the cost-effectiveness of chemoprophylaxis for children, and the coverage of antenatal-care services affects the cost-effectiveness of prevention in pregnancy. These findings imply that it would be more cost-effective to direct resources to areas in which, for example, there is good antenatal-care coverage, or use of nets is already high, which are likely to be better-off areas. Such direction of resources, however, ignores equity objectives, which require that benefits accruing to the worst-off groups are given greater weight than those accruing to the better-off groups. Hence information on the cost-effectiveness of interventions must always be considered in conjunction with information on the characteristics of those who will benefit.[30]

Because of the rapid growth in drug resistance[31] and the likely development of insecticide resistance,[32] potential changes in cost-effectiveness over time must be taken into account. Moreover, there is concern that wide-scale chemoprophylaxis could substantially increase the growth of drug resistance,[33] which would lower the cost-effectiveness of this intervention and possibly threaten the provision of effective case management. In addition, long-term use of preventive interventions in areas of high malaria transmission could decrease the rate at which immunity is acquired, leading to increased malaria morbidity and mortality in older age-groups. This mortality rebound in later childhood might cancel out some of the benefits of the mortality decreases achieved in younger children.[34] The potential impact of rebound mortality on the cost-effectiveness of insecticide-treated nets is explored elsewhere.[35]

Cost-effectiveness analyses help to identify interventions that use resources efficiently, but information on total costs is also needed to assess affordability. Some interventions are inexpensive (figure 3): prevention in pregnancy, improvement of compliance with treatment, and improvement of the availability of second-line and third-line drugs would each absorb less than 1% of the existing budget. Achievement of high coverage with an intervention to prevent childhood malaria, however, has a high total cost. For example, full coverage of children younger than 5 years with insecticide-treated nets would cost around 24% of the existing health-care budget. The same coverage with residual spraying would be more expensive, costing about 27% of the existing budget with one spraying round per year, and 55% with two rounds. In addition to the difficulties of financial feasibility, the implementation of interventions presents many operational and logistic challenges. Innovative approaches are needed to tackle low rates of net re-treatment, and strong management capacity is required to run an effective and well-timed spraying programme, or to supervise and support a network of village health workers.

The political will currently exists to ensure a substantial decrease in malaria mortality. The central message from our analysis is that all the interventions assessed would be cost-effective ways to bring about such decreases, despite the narrow age range for health benefits incorporated in the preventive models, which excluded benefits for older children and adults. To set these cost-effectiveness ratios in context, other studies have found the cost-effectiveness of measles vaccination to be $2–17 per DALY averted, oral rehydration therapy $41–408, onchocerciasis vector control $120–230, and the medical management of hypertension more than $2000 (1995 US$).[36] Although the methods of calculation may not be strictly comparable, malaria control is clearly one of the most cost-effective interventions.

In view of the many pressing needs and limited resources, a package of interventions to substantially decrease the malaria burden is evidently not affordable to very-low-income countries through government finance alone. Although there is scope for increased private-sector involvement, the most vulnerable and impoverished groups in Africa will not be reached with effective prevention and treatment without substantial assistance from external donors. Even if these financial resources were generated, important operational challenges would still have to be addressed, including obtaining high coverage with preventive interventions and strengthening peripheral health services.

Contributors

Anne Mills initiated and coordinated the research and supervised all stages. Catherine Goodman and Paul Coleman reviewed the literature, designed the models, and did the analysis. All investigators contributed to the writing of the paper.

Acknowledgments

This study was supported by the Global Forum for Health Research through a grant provided by the World Bank. Anne Mills and Catherine Goodman are members of the London School of Hygiene and Tropical Medicine Health Economics and Financing Programme, which is supported by the UK Department for International Development. This project was undertaken in collaboration with the London School of Hygiene and Tropical Medicine Malaria Programme and the London/Liverpool Malaria Consortium. We also thank the many researchers and control staff who provided technical advice.

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