The evidence base on the cost-effectiveness of malaria control measures in Africa

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This review assesses the range and quality of the evidence base on the cost-effectiveness of malaria prevention and treatment in sub-Saharan Africa. Fourteen studies are reviewed, covering insecticide-treated nets, residual spraying, chemoprophylaxis for children, chemoprophylaxis or intermittent treatment for pregnant women, a hypothetical vaccine, and changing the first line drug for treatment. The available evidence provides some guidance to decision-makers. However, the potential to inform policy debates is limited by the gross lack of information on the costs and effects of many interventions, the very small number of cost-effectiveness analyses available, the lack of evidence on the costs and effects of packages of measures, and the problems in generalizing or comparing studies that relate to specific settings and use different methodologies and outcome measures.

Malaria prevention

The majority of studies evaluated interventions to prevent malaria. Eleven evaluations provided information on the cost-effectiveness of insecticide-treated nets (ITNs), residual spraying, chemoprophylaxis for children, and chemoprophylaxis or intermittent treatment for pregnant women. In addition, two studies estimated the potential cost-effectiveness of a hypothetical vaccine. No CEA were found of untreated nets, other methods of personal protection (such as coils and...
sprays), environmental management, or the control of epidemics.

**Insecticide-treated nets**

A series of randomized controlled trials have demonstrated that ITNs are highly effective in preventing malaria in children under 5 years of age. Bednets are treated with a pyrethroid insecticide, which repels and kills mosquitoes and so inhibits their feeding on humans. Whilst nets normally last for several years, the efficacy of the insecticide gradually wears off over time, so it is necessary to retreat the nets regularly. Implementation remains very limited in SSA:

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Note: DYLG = discounted year of life gained
only The Gambia runs a national programme (for net treatment).

Three CEAs were conducted alongside the trials, in The Gambia\(^2\) (here called Gambia 1), Ghana,\(^13\) and Kenya.\(^14\) Another Gambian study\(^15\) evaluated the National Impregnated Bed Net Programme (Gambia 2). In The Gambia, net coverage in the communities was already high, so the intervention involved net treatment only. By contrast, in Ghana and Kenya, initial net coverage was low and nets had to be both provided and treated. All of the studies evaluated a similar public sector delivery mechanism for communal net treatment. They all involved a comprehensive costing from a societal perspective, and they discounted years of life gained at 3%. The studies in The Gambia and Kenya used a discount rate of 6% for capital costs, compared with 3% for the Ghana study, but as capital costs made up a small component of total costs in each case, recalculating the results with a uniform discount rate makes very little difference to the results. The Gambia 2 study reported a net cost-effectiveness ratio, incorporating savings in treatment and prevention expenditure and reduced production loss. To maintain consistency with the other studies, these results are quoted as gross ratios, excluding these cost savings.

The gross cost per death averted (DA) was $219 in Gambia 1 and $665 in Gambia 2, much lower than the ratios of $2112 found in Ghana and $2958 in Kenya. The main reason for the lower ratios in the Gambian studies was that the cost of the nets was not included as they were not provided as part of the intervention. In addition, the trials in Ghana and Kenya involved two rounds of insecticide treatment per year, whereas under the shorter Gambian transmission season, only one round was required.

Gambia 1 was more cost-effective than Gambia 2. Gambia 1 had higher costs per child protected ($6.58 versus $1.35), because the insecticide price was higher, higher doses of insecticide were used, and more nets were treated per child (2.8 nets per child aged 6–59 months in Gambia 1; one net per child aged 1–9 years in Gambia 2, equivalent to two nets per child under 5 years). However, the effectiveness of Gambia 1 was greater: a reduction in all-cause mortality of 42% (children aged under five),\(^16\) compared with 25% in children aged 1–9 years in Gambia 2 (or 19% in children under five).\(^17\) Reductions on the scale of that achieved in Gambia 1 have not been replicated elsewhere.

Comparing the two trials that involved provision of nets and two treatments per year, the Ghana trial was more cost-effective than the trial in Kenya. This was partly due to higher costs for staff and the sensitization and awareness campaign in Kenya ($0.61 per net in Kenya compared with $0.20 in Ghana). In addition, although the percentage reduction in child mortality was higher in Ghana than in Ghana (33% for children aged 1–4 years in Ghana,\(^18\) 17% for children aged 6–59 months in Ghana\(^19\)), underlying mortality rates were higher in Ghana. Without nets, the baseline mortality rate per thousand in different zones ranged from 23 to 27.9 for children aged 6–59 months, compared with between 13.2 and 15.8 in Kenya for children aged 1–59 months. As a result, a given percentage reduction in mortality averted a much greater absolute number of deaths in Ghana.\(^20\) This factor also partly explains the better performance of Gambia 1 compared with Gambia 2. In Gambia 1, the underlying mortality rate for children aged 1–4 years was between 24.2 and 47.6, whereas in Gambia 2 it was 23.6 for children aged 1 and 2, and 11.4 for children aged 3 and 4.\(^16\)\(^17\)

There are some reasons to expect these cost-effectiveness estimates to be conservative. The studies included only the benefits of reduced mortality to children under five, or under ten in the case of Gambia 2, ignoring the impact on morbidity and mortality of adults. Whilst most adults are at a much lower risk of mortality and morbidity from malaria, this is not the case for pregnant women and non-immunes, such as migrants. In addition, all the evaluations used permethrin as the insecticide, but other pyrethroids are now available, such as deltamethrin and lambdacyhalothrin, which last longer and may reduce the number of retreatments required per year.

On the other hand, the artificial settings of the studies may have produced estimates of cost-effectiveness that are over-optimistic for an ongoing programme. Three of the four evaluations are based on trials and, whilst Gambia 2 was an evaluation of the national programme, the situation was still very controlled and not typical of an operational setting. Two modelling studies have been conducted which allow the importance of this to be explored by evaluating the impact of varying key factors, such as compliance.

Evans et al.\(^21\) estimated the cost per discounted year of life gained (DYLG) of providing nets and insecticide for a cohort of newborns facing standard West African death rates. They assumed a reduction in all-cause mortality of 25% for children aged 0–4 years, and used Gambia 1 cost data, adding a relatively high price per net of over $9. The results demonstrated the important influence of compliance and the number of nets distributed per child on cost-effectiveness. With 100% compliance and three nets distributed per child, the cost per DYLG was $58. Reducing compliance from 100 to 50% led to a doubling in the cost-effectiveness ratio to $118. Reducing the number of nets per child, from three to 0.5, with 50% compliance, reduced the cost per DYLG almost six-fold, from $118 to $20. However, the potential impact on effectiveness of reducing the number of nets used by other household members was not considered. It is possible that the effectiveness found in the trials was partly due to mass killing of the mosquito population. Although such an effect was not found in The Gambia, it may be important in other settings.\(^22\)–\(^25\) If the mass effect were important, restricting treated net use could reduce effectiveness in the target group. Moreover, it is unclear whether a targeted approach would be feasible in practice. For example, in Ghana, nets were initially not provided for men, but this was later found to be necessary to ensure that nets were not diverted to adult males, leaving children in the target group unprotected.\(^13\)

A second modelling study, by Graves,\(^26\) used a decision tree approach to estimate the cost-effectiveness of net treatment. The model followed a cohort of Gambian children from birth to 5 years, and assumed a reduction in all cause mortality for
children aged 1 month to 5 years of 35%, varied between 17 and 63% in the sensitivity analysis, and coverage of 75%, varied between 60 and 90%. The provider cost per child was extrapolated from the Gambia 1 data (cost of the nets not included). The cost per child DA was found to be $829 in the base case, varying from $447 to $2117 in the sensitivity analysis.

The authors of both the trial-based and modelling studies all came to the broad conclusion that ITNs were a highly cost-effective use of resources, but several questions remain unanswered about their cost-effectiveness in practice. Firstly, all the studies considered one particular delivery method: a government programme established to purchase insecticide and organize net retreatment, and where necessary distribute nets, with no charges for users who provided only limited amounts of labour and resources such as water and detergent. No CEAs were identified on other delivery modes, such as the use of social marketing, the involvement of the private sector, or the individual treatment of nets at home. Secondly, even the lowest compliance rates included in the models, of 50% (Evans et al.) and 60% (Graves), may overestimate the level achievable in practice. Compliance encompasses both regular net retreatment and correct net use. Children may not use nets if they sleep outside in hot weather, if the nets are used for other family members or the nets are taken away, destroyed or sold. Retreatment rates have been very low under operational conditions, rarely exceeding 25%. Moreover, the analyses assumed that the relationship between compliance and effectiveness was linear, but if the mass effect was important, effectiveness would increase in a non-linear fashion with disproportionately greater effects at higher compliance levels. The models would then overestimate the effectiveness of ITNs at lower levels of compliance.

Residual spraying

Residual house spraying involves the treating of all interior walls and ceilings with an insecticide, and is effective against mosquitoes that favour indoor resting before or after feeding. Advocated as the mainstay of malaria eradication programmes in the late 1950s and 1960s, it remains a major component of control programmes in southern African states, though many countries have abandoned or curtailed their spraying activities due to disillusionment over the failure to achieve eradication, concerns over the safety and environmental impact, and administrative, managerial and financial constraints on implementation.

Two cost-effectiveness estimates are available. Firstly, data from a trial conducted in Garki, Nigeria were used by Barlow and Grobar to estimate a cost per case prevented of $342.30 This result is difficult to interpret because the costs covered both research and implementation activities, and appear to have included some costs of the accompanying drug administration and larviciding which were also part of the Garki trial.

Secondly, Walsh and Warren provided an estimate of the cost per DA of residual spraying.31 A simple model was used to calculate average estimates for a rural area of SSA with twice yearly DDT spraying. They assumed reductions in the crude death rate of 40% and the infant mortality rate of 50%, based on trials in the 1950s and 1960s, and derived a cost per adult DA of $584, and a cost per infant DA of $1402. The cost data used in these estimates were based on a WHO report and covered adult mosquito and larval control in a ‘small area of economic importance’. It is not possible to isolate the costs of spraying alone, and it is unlikely that the average costs for an area of economic importance, such as an agricultural development project, would be appropriate to a typical sub-Saharan rural area. It is also not clear how these cost estimates were derived, nor whether they included capital as well as recurrent costs.

Neither study can therefore be considered an accurate estimate of the cost-effectiveness of spraying. Moreover, the estimates may not be good predictors of cost-effectiveness in current programmes. Firstly, they both consider the cost-effectiveness of spraying with DDT, although other insecticides are increasingly used. Secondly, the trials in the 1950s and 1960s would have achieved very high levels of compliance, but in a contemporary operational setting people may object to the spraying because of the inconvenience, the residue left on the walls, the smell, or fears about the health effects of inhaling the fumes. For example in Namibia, householders have refused entry to the spray teams, and in Zimbabwe 21% of villagers refused to have some rooms in their homes sprayed. Thirdly, underlying mortality rates in SSA have fallen dramatically over the last 30 to 40 years, which may reduce the absolute number of lives saved by the intervention. Finally, WHO now recommends spraying only in certain circumstances (e.g. for control of epidemics, areas of economic importance, refugee camps and initial protection of non-immune settlers in development areas) where both costs and effectiveness are likely to differ from those for more general use. No estimates were identified for such targeted approaches.

Chemoprophylaxis for children

Whilst it is generally agreed that administration of chemoprophylaxis to the whole population is not appropriate, targeted programmes have been advocated for vulnerable groups, such as non-immune travellers, pregnant women and children under 5 years of age. This strategy is not currently implemented for children in SSA, although large-scale programmes have been undertaken in several countries in the past, such as Senegal, Ghana, Niger, and Burkina Faso. The Gambia 1 ITN trial also evaluated the cost-effectiveness of adding chemoprophylaxis to a net treatment programme. Maloprim (pyrimethamine and dapsone) was distributed by village health workers (VHWs) every week during the rainy season to children aged 6–59 months. The addition of chemoprophylaxis did not reduce mortality further, so the cost per DA increased from $219 with net treatment alone to $300 with the combined intervention. However, there was a marked incremental reduction in morbidity, reducing the cost per case averted from $33 to $23.

The Gambia 1 cost data were also used to estimate the cost-effectiveness of chemoprophylaxis alone. Effectiveness
Cost-effectiveness of malaria control measures

Data were taken from a controlled trial in rural Gambia,\(^3^9\) which evaluated the provision of fortnightly Maloprim by VHWs. For children aged 6–59 months, there was a reduction in all-cause mortality of 49% and a reduction in the incidence of clinical episodes of 73%. The cost per child DA was $167, leading the authors to conclude that chemoprophylaxis appeared to be more cost-effective than net treatment in The Gambia, although they acknowledged that maintaining compliance might require much more substantial investment in other settings. The average compliance in the Gambia trial was 60%, but when the programme was evaluated over a five-year period it was found to have dropped to 33.6% overall.\(^4^0\)

The authors also noted that wide-scale chemoprophylaxis was not generally recommended due to the dangers of accelerating the growth of drug resistance and potentially impairing acquired immunity. In the areas studied in The Gambia, a network of volunteer VHWs was well established, but in much of SSA this is not the case. Operating a programme for the community distribution of prophylaxis would require the establishment of a VHW cadre, which could significantly add to the incremental costs of providing the intervention.\(^4^1\)

**Potential malaria vaccines**

Two analyses have modelled the potential cost-effectiveness of a malaria vaccine. Graves\(^2^6\) assumed that (1) a vaccine could be given in three doses before the age of six months through the Expanded Programme on Immunization (EPI), (2) it would remain effective up to the age of 5 years, and (3) it would reduce all cause mortality by 20% (varied between 10 and 30% in sensitivity analysis). Coverage was assumed to be 75%, varied between 60 and 90%. Costs were based on estimates for delivering hepatitis B vaccine in The Gambia, assuming a price per vaccine of $1.17. The estimated cost per DA was $294, varying from $163 to $737 in the sensitivity analysis, leading the author to conclude that such a vaccine would be more cost-effective than insecticide treatment of nets in The Gambia.

A similar analysis was reported by WHO,\(^4^2\) which estimated the cost per DYLG by a vaccine under a variety of assumptions about the duration of protection, the price per child, and whether the strategy could be delivered within the existing EPI schedule. For example, in high transmission areas under the author’s ‘best’ scenario, when the vaccine could be added to the existing EPI schedule at an incremental cost of $1, had a duration of 5 years, and reduced all-cause mortality by 30% in children aged 0–4 years, the cost per DYLG would be $0.36. Even under the ‘poor’ scenario, where the vaccine had a 1-year duration, could not be incorporated under EPI, and instead had to be administered in five annual courses with a total cost of $15 per child, the cost per DYLG was still below $23.

**Chemoprophylaxis in pregnancy**

Pregnant women are particularly vulnerable to malaria. Infection may cause harmful effects for the mother, and placental parasitaemia retards the growth of the foetus and increases the prevalence of low birth weight (LBW), the proportion of newborns weighing less than 2500 g.\(^4^3\) This is of particular concern because LBW is associated with increased neonatal mortality.\(^4^4\) In areas of high transmission, the effects are most marked during the first pregnancy (primigravidae).\(^4^5\) Chemoprophylaxis, or presumptive intermittent treatment with antimalarials during pregnancy, has been shown to reduce the risk of malaria infection in all pregnant women and to increase significantly the birth weight of babies born to primigravidae.\(^4^6\) Although WHO recommends that all pregnant women in endemic areas receive regular chemoprophylaxis, in a survey of four countries only 1–18% of women reported taking adequate weekly doses.\(^4^7\)

Two studies have used data from Malawi to investigate the cost-effectiveness of chemoprophylaxis or intermittent treatment provided during antenatal care (ANC) visits. Heymann et al.\(^4^8\) modelled the cost-effectiveness of chloroquine (CQ) chemoprophylaxis, based on a protective efficacy of 23% in preventing parasitaemia (obtained from women who were supervised taking their drugs) and 36% compliance (based on urine samples of women visiting antenatal clinics), giving an actual protective efficacy of 8%. This was combined with drug-cost data to give a cost per case prevented of $15, which the authors concluded ‘is an unacceptably high cost in much of Africa’. However, they noted that if prophylaxis were restricted to women in their first and second pregnancies, the drug cost per case prevented would be reduced to less than $6.

Schultz et al.\(^4^9\) used a decision-analysis model to assess the relative cost-effectiveness of three antenatal drug regimens in reducing LBW of babies born to women in their first or second pregnancies (health benefits to mothers were not considered). Again, only drug costs were included. Based on data from the Mangochi Malaria Research Project, placental malaria infection rates were assumed to be 38% with no antimalarials. With a treatment dose of CQ at first antenatal visit, followed by CQ prophylaxis weekly until delivery, the infection rate was assumed to be 32%; with an initial treatment dose of sulfadoxine-pyrimethamine (SP) followed by CQ prophylaxis, the infection rate was assumed to be 26%; and with two treatment doses of SP, one given at first antenatal visit and one at the beginning of the third trimester, the infection rate was assumed to fall to 9%. It was assumed that there was a 28% LBW rate with placental malaria and 20% without. They found a cost per LBW case prevented of $10 for the regimen of two SP treatment doses, compared with $67 for the regimen of initial SP treatment followed by weekly CQ prophylaxis, and $123 for initial CQ treatment followed by weekly CQ. The results were extrapolated to estimate the cost per DA by assuming that infant mortality was 128/1000 for babies of adequate weight, and 257/1000 for LBW babies. This gave a cost of $81 per infant DA for the two doses of SP, $522 for the SP treatment and CQ prophylaxis regimen, and $951 for the CQ treatment and prophylaxis option.\(^5^0\) Partly in response to this analysis the Malawi Ministry of Health changed the national policy from weekly CQ prophylaxis to two intermittent SP treatments in 1992.\(^4^7\)

The differences in the relative cost-effectiveness of the three regimens stem from three factors. Despite the lower costs per treatment dose for CQ compared with SP, the costs of the two
regimens involving weekly CQ prophylaxis are higher per pregnancy. It was assumed that SP was more effective in reducing the placental infection rate because resistance to CQ was higher, and compliance with CQ prophylaxis was assumed to be lower, at only 35%, compared with 100% compliance with SP. Univariate and multivariate sensitivity analyses were used to demonstrate that the relative cost-effectiveness of the three regimens was not changed by varying CQ efficacy, SP efficacy, or CQ compliance over ‘a wide range of parameter estimates’. However the lowest SP efficacy considered in the sensitivity analysis was an 18% infection rate amongst the intervention group, still markedly better than the regimens involving CQ. The analysis did not explore the impact of higher levels of SP resistance on relative cost-effectiveness.

No studies were identified with full costings of the delivery of these interventions, preventing direct comparison with cost-effectiveness ratios for other malaria control strategies. Moreover the analyses were based on the assumption that ANC services were already in place. Whilst for Malawi over 90% of births receive at least one ANC visit, this is under 60% in Burkina Faso and Nigeria, and under 30% in Niger.\(^{55}\) The incremental costs to both the facility and to women would be much greater if it were necessary to set up an entirely new ANC service in order to implement the intervention.

**Malaria treatment**

Two studies were identified on the choice of drug for the treatment of uncomplicated malaria. For decades CQ has been the official first line drug in nearly all African countries as it is cheap, effective and safe, causing only minor side effects. CQ resistance first appeared in Africa in the late 1970s. It spread very slowly at first, but from the mid–1980s the rate of growth accelerated rapidly, and it is now common in practically all endemic countries in SSA.\(^{52}\) Resistance has made it increasingly difficult to provide effective treatment and has been associated with a rise in malaria related mortality,\(^ {53}\) leading to considerable debate over when the first line drug should be changed, and the choice of replacement drug.\(^ {54}\)

Sudre et al.\(^ {55}\) used decision-tree analysis to investigate the cost-effectiveness of three alternative drugs for the treatment of children under five at primary health care facilities in a hyper- or holoendemic area of SSA. They considered CQ, amodiaquine (AQ) and SP, using case fatality rates (CFRs) derived from a Delphi survey of 19 malaria experts. Compliance was assumed to be 80% with CQ and AQ, and 95% with SP, based on drop-out and loss-to-follow-up rates from in vivo drug trials. The authors combined these parameters with estimates of the proportion of fever episodes associated with parasitaemia, the probability of side-effects, and drug costs to calculate the cost per DA for each drug. The costs of the first line drugs only were included, excluding the costs of staff time, equipment, and other overheads, so it is not possible to compare the results with the cost per DA by preventive interventions.

In the absence of drug resistance, the drug cost per DA was $1.47 with CQ, $1.70 with SP and $2.35 with AQ. The cost per DA with CQ rose to $1.49 in the ‘low resistance’ scenario (RI 23%, RII 4%, RIII 0%), and $2.56 in the ‘high resistance’ scenario (RI & RII 57%, RIII 34%). The analysis showed that more deaths were prevented per dollar spent on SP than for CQ as long as the level of RIII CQ resistance was greater than 14%. The authors concluded that SP would be the drug of choice even in the ‘no resistance’ scenario if the value of a death prevented was more than $2.66. (AQ was the least cost-effective drug in all scenarios examined.)

Sensitivity analysis showed that the threshold of CQ resistance at which SP became more cost-effective remained little changed regardless of the parameters used for the CFR, side-effects, and risk of malaria infection (assuming no resistance to SP). Drug costs had an important impact on the results; if SP were 14% cheaper it would be as cost-effective as CQ even in the no-resistance scenario. Since this article was published, there has been a relative reduction in the cost of SP compared with CQ, to the point where the cost per treatment dose is approximately equal,\(^ {56}\) further strengthening the case for SP. However, changing the initial rate of resistance to SP also had an important impact on the results. For example, if there is an initial level of 10% RIII resistance to SP, the threshold of CQ resistance at which SP became more cost-effective increased to over 20%. The model does not allow for the possibility of increased resistance to SP once it is adopted although there is widespread concern that this will be rapid.\(^ {57}\)

Schapira et al.\(^ {58}\) used a mathematical model to incorporate the growth of drug resistance by assuming that once a drug is introduced on a wide scale, treatment failure increases exponentially at a rate of 11% per annum. Assuming that the first line drug would initially be CQ, they estimated when it would be appropriate to switch to SP, and from there to mefloquine and finally halofantrine, in order to minimize total costs over a 27-year period. The model was constrained so that all four drugs had to be used in the 27-year period for at least one year in the specified sequence, and that SP and mefloquine had to be used for an equal length of time. Each death was valued at US$8843 to represent the loss in lifetime production, so the study was structured as a cost-benefit analysis rather than as a CEA. They concluded that it would be appropriate to shift to SP after 5 years, when the proportion of treatment failures with CQ was 42%, and then to use SP and mefloquine for 10 years each, and halofantrine for 2 years. No sensitivity analysis was conducted to assess how robust the conclusions were to changes in assumptions such as the discount rate used, and time period considered.

The model makes an important contribution in attempting to incorporate the growth of resistance over time, which is a major concern of policy-makers. An inherent disadvantage is that the lack of actual data on the development of resistance necessitates the use of arbitrary assumptions (not varied in the model). In reality the development of resistance is a very complex phenomenon, dependent on a wide variety of influences that are not well understood, making its future path very difficult to predict. For example, it is possible that the growth rate of resistance to different drugs will vary, and that growth rates will vary over time. A further limitation is the assumption that the proportion of treatment failures to each
drug when first adopted is 2%, except for halofantrine as some cross-resistance is assumed with mefloquine. This does not allow for the possibility that resistance will grow to a drug whilst it is not the official first line drug. As between 40 and 60% of antimalarials in SSA are distributed through private providers,39 if a drug becomes widely available in the private sector it is likely that resistance will grow rapidly, even if it is not part of the official regimen.

No CEAs of treatment were identified with full costings, and no evaluations were found on interventions other than changing the first line drug, or on any interventions to improve the case management of severe malaria.

Discussion
To use the results, policy-makers must at a minimum be confident that the studies are comparable, meaning that they included a comparable range of costs and effects, and followed a similar methodology, for example to value community time, and discount costs and effects. In addition, there must be a measure of effectiveness that is common across the interventions being compared, such as DA or DYLG. The results of studies that quote a cost per DA or per DYLG are shown in Table 2.

For interventions to prevent malaria in childhood, estimates of the cost per DYLG are available for ITNs and a hypothetical vaccine. For insecticide treatment of nets, results ranged from $9–$27, and for provision and treatment of nets from $10–$118. For the vaccine, one study provided ranges from $0.36–$41 in high transmission areas and from $5–$621 in low transmission areas. The identification of the most cost-effective intervention was therefore not clear cut, and depended on the assumptions used. Estimates of the cost per DA were available for ITNs, a hypothetical vaccine and chemoprophylaxis for children. For insecticide treatment of nets, results ranged from $167–$2117, for provision and treatment of nets from $992–$3120, for the vaccine from $163–$737, and for chemoprophylaxis one point estimate of $167 was available. Again there is overlap in the ranges for the vaccine and insecticide treatment of nets, but the vaccine appears more cost-effective than provision and treatment of nets. However, in the study of vaccines by Graves,28 neither the possibility that delivery could not take place through EPI, nor a vaccine duration of under 5 years, were considered. Moreover, as a vaccine is not currently available, these results are more relevant for the identification of research priorities than the current selection of interventions. Chemoprophylaxis for children appears more cost-effective than ITNs. However, the possibility that the provision of chemoprophylaxis on a wide scale could significantly increase the growth of drug resistance40 is not allowed for, although this could reduce the cost-effectiveness of the intervention and possibly threaten the provision of effective case management. Due to the considerable overlap in these results, it is not possible to identify which intervention represents the best value for money. However, it is clear that the results for all of these interventions would be considered cost-effective according to the guideline that any intervention with a cost per DALY or DYLG below $150 is an attractive use of resources in a low-income country.42

The studies by Schultz et al.50 on antenatal chemoprophylaxis, and Sudre et al.55 on treatment of children, provide a cost per DA, but are not directly comparable to the studies on prevention in childhood because the costings are partial, including drugs only. However, some tentative interpretations are possible. The drug cost per infant DA by administration of prophylaxis during pregnancy in Malawi ranged from $79 to $951. The epidemiological situation in Malawi could be compared with the ‘high resistance’ scenario in the study on treatment for children, where the drug cost per DA ranged from $0.31 to $5.67. Although it is not clear how similar the non-drug costs of these two interventions would be, for all plausible assumptions, the treatment of children with malaria is a more cost-effective way to prevent childhood deaths than the provision of prophylaxis to expectant mothers. As there is a broad consensus that curative treatment should always be made available to populations affected by malaria,36 it is not clear that the choice between these two interventions would represent a relevant policy decision. Prevention in pregnancy would be better compared with expenditure on other preventive measures, such as ITNs, or on strategies to extend access to treatment or improve its quality. However the lack of full cost analyses of antenatal prevention or improvements in case management precludes this at this stage.

If these analyses are to be used by policy-makers, they must be confident that the results are not only comparable, but also applicable to an operational situation, and appropriate for their geographical setting. Many of the studies are based on trial settings, which may be unrepresentative of routine service delivery. Whilst costs are generally adjusted to remove any research-related expenses, compliance is likely to be much higher in trial settings, giving an over-optimistic estimate of effectiveness and cost-effectiveness. The modelling studies attempted to adjust for realistic levels of compliance but, as discussed above, the relationship between compliance and effectiveness can be difficult to predict.

It may also be inappropriate to generalize results from one region to another. Effectiveness may vary due to differences in epidemiological conditions, demographic factors, immunity levels and drug resistance, and differences in education levels and local cultural factors may affect compliance. Costs may vary depending on the scale of the intervention, the price of inputs such as salaries, the level of existing infrastructure, and the population density. In addition, the acceptability of the intervention to local people, and the availability of managerial capacity, will affect both costs and effectiveness. These variations may alter the relative cost-effectiveness of interventions in different settings. However, the available studies do not provide a systematic analysis of variation in cost-effectiveness across different epidemiological and economic zones. Country coverage is haphazard, and relates to where the most accurate research institutions are located: seven of the 14 studies identified used data from either The Gambia or Malawi. Finally, in view of the rapid growth in drug resistance,58 the likely development of pyrethroid insecticide resistance,64 and the possible reduction in the rate of immunization with effective protection,62 it is essential to consider potential changes in cost-effectiveness over time, but this issue has been relatively neglected.
Table 2. Cost-effectiveness results for interventions using comparable outcome measures (1995 US$) (sensitivity analysis results in brackets)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Area studied and study year</th>
<th>Intervention(s) evaluated</th>
<th>Cost per child death averted (DA)</th>
<th>Cost per DYLG</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevention in Childhood</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Insecticide treatment of bednets and chemoprophylaxis</td>
<td>$300 ($246–$333)</td>
<td>$13 ($13–$20)</td>
<td>Sensitivity analysis for cost per DYLG based on increasing discount rate on YLG to 6% and reducing effectiveness by 10%.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gross costs $665</td>
<td>Gross costs $27</td>
<td></td>
</tr>
<tr>
<td>Binka et al. 1997&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Ghana, 1993–5</td>
<td>Provision and insecticide treatment of bednets</td>
<td>$2112 ($992–$2289)</td>
<td>$77 ($37–$84)</td>
<td>Sensitivity analysis based on increasing discount rate on costs to 10%, reducing number of treatments to one per year, reducing the insecticide cost by 50%, and reducing the number of nets distributed.</td>
</tr>
<tr>
<td>Some 1998&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Kenya, 1993–4</td>
<td>Provision and insecticide treatment of bednets</td>
<td>$2958 ($2838–$3120)</td>
<td>–</td>
<td>Sensitivity analysis based on varying discount rate on costs from 3% to 10%.</td>
</tr>
<tr>
<td>Evans et al. 1997&lt;sup&gt;21&lt;/sup&gt;</td>
<td>Africa (Gambia cost data), 1996</td>
<td>Provision and insecticide treatment of bednets</td>
<td>–</td>
<td>$10–$118</td>
<td>Quoted variation based on varying compliance from 50 to 100%, age group protected from 0–4 years to 1–4 years, number of nets per child from 0.5 to 3, price of net from $9 to $33, life expectancy at birth from 50 to 84 years, and including 10 days for morbidity per episode.</td>
</tr>
<tr>
<td>Graves 1998&lt;sup&gt;26&lt;/sup&gt;</td>
<td>The Gambia, 1990</td>
<td>Insecticide treatment of bednets</td>
<td>$829 ($447–$2117)</td>
<td>–</td>
<td>Quoted variation based on varying coverage from 60 to 90% and reductions in all cause mortality from 17 to 63% for ITNs and from 10 to 30% for vaccine.</td>
</tr>
<tr>
<td>Hypothetical vaccine</td>
<td></td>
<td></td>
<td>$294 ($163–$737)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>WHO 1996&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Africa, 1996</td>
<td>Hypothetical vaccine</td>
<td>High transmission $0.36–$41</td>
<td>–</td>
<td>Quoted variation based on varying duration of protection from 1–5 years, the cost per child from $1–$15.</td>
</tr>
<tr>
<td>Low transmission $5–$621</td>
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</table>
Table 2. Continued

<table>
<thead>
<tr>
<th>Reference</th>
<th>Area studied and study year</th>
<th>Intervention(s) evaluated</th>
<th>Cost per child death averted (DA)</th>
<th>Cost per DYLG</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevention in Pregnancy</strong></td>
<td>Malawi, 1992 costs</td>
<td>Antenatal treatment and chemoprophylaxis: 2 SP treatments, weekly CQ prophylaxis</td>
<td>$81 ($79–$352)</td>
<td>–</td>
<td>Only drug costs were included. Sensitivity analysis based on varying ANC attendance, compliance with both drugs, SP cost, number of weeks of CQ prophylaxis, and CQ efficacy.</td>
</tr>
<tr>
<td>Schultz et al. 1995</td>
<td></td>
<td>1 SP treatment, weekly CQ prophylaxis</td>
<td>$522 ($212–$812)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 CQ treatment, weekly CQ prophylaxis</td>
<td>$950 ($317–$951)</td>
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<tr>
<td><strong>Treatment</strong></td>
<td>Africa, 1991</td>
<td>Drug treatment for children: CQ</td>
<td>–</td>
<td>–</td>
<td>Only drug costs were included. Sensitivity analysis based on varying probability of lethal and minor side-effects, probability of malaria infection, case fatality rate and compliance. No resistance scenario: no resistance to any drugs. Low resistance scenario: CQ – RI 23%, RII 4%, RIII 0%; AQ – RI 3%; SP – no resistance. High resistance scenario: CQ – RI &amp; RII 57%, RIII 34%; AQ – RI &amp; RII 60%, RIII 7%; SP – no resistance.</td>
</tr>
<tr>
<td>Sudre et al. 1992</td>
<td></td>
<td>No resistance scenario</td>
<td>$1.47 ($0.21–$3.36)</td>
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<tr>
<td></td>
<td></td>
<td>Low resistance scenario</td>
<td>$1.49 ($0.22–$3.36)</td>
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<tr>
<td></td>
<td></td>
<td>High resistance scenario</td>
<td>$2.56 ($0.31–$4.34)</td>
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<tr>
<td></td>
<td></td>
<td>AQ</td>
<td>$2.35 ($0.34–$5.40)</td>
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<tr>
<td></td>
<td></td>
<td>No and low resistance scenarios</td>
<td>$2.89 ($0.40–$5.67)</td>
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<tr>
<td></td>
<td></td>
<td>High resistance scenario</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>SP</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>All resistance scenarios</td>
<td>$1.70 ($0.25–$3.92)</td>
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</tbody>
</table>
More studies are evidently needed, but this takes time and it will never be possible to do studies in every possible situation. This argues for a modelling approach, with a uniform framework for all interventions to make the results as comparable as possible and to allow for changes across regions, over time, and between trial and operational settings. We have recently developed such models for ITNs, residual spraying, chemoprophylaxis for children, CQ prophylaxis and SP intermittent treatment in pregnancy for primigravidae, and several interventions to improve treatment, drawing on all available SSA cost and effectiveness data, and calculating ranges for the cost per DALY averted by each intervention. This work demonstrates that highly cost-effective interventions exist for both prevention and treatment; that approaches to improving treatment are likely to be highly cost-effective; and that given the uncertainty and variation involved, the choice between childhood preventive interventions is not clear-cut due to the considerable overlap in their cost-effectiveness ranges.

Several challenges in using cost-effectiveness estimates for policy-making need emphasis.

1. Lack of information on costs and effects of interventions

For many interventions, information on costs and effects is very limited. The studies of ITNs are the only analyses that provide a good basis for assessing allocative efficiency. Data to construct similarly comprehensive and methodologically sound estimates for other interventions are currently lacking and urgently required. For example, evidence is inadequate on the health impact and costs of residual spraying, and interventions to improve treatment, including the Integrated Management of Childhood Illness (IMCI), an approach currently being piloted which aims to improve the treatment of the most common childhood diseases and conditions, including malaria. For some interventions, such as epidemic surveillance and preparedness, environmental control, and the treatment of severe malaria, data are practically non-existent. Even for interventions where data are relatively good, such as ITNs, information is lacking on the costs and effects of alternative delivery strategies such as the use of social marketing and individual retreatment kits.

2. Lack of estimates of the cost-effectiveness of packages of interventions

Most studies consider the costs and effects of individual interventions, but in practice malaria control involves the selection of a package of complementary measures. The effectiveness of interventions implemented together is difficult to estimate. For example, the total effects of combined interventions may be less than the sum of their incremental effectiveness when implemented alone, as in the case of chemoprophylaxis combined with ITNs in The Gambia. The incremental cost of interventions could also be lower when implemented together if resources were shared and therefore used more efficiently. Policy-makers currently lack both the data on costs and effects of packages, and the models with which to predict them.

3. Lack of comparable estimates for other health care interventions

To allocate resources across the health care sector appropriately, policy-makers need to compare the cost-effectiveness of malaria prevention and treatment interventions with those for other health care problems, which requires the use of a standardized cost-effectiveness methodology. Several attempts have been made to develop standardized guidelines, such as the ‘reference case’ proposed by Gold et al., and the framework currently under development by the Global Forum for Health Research. However, until one such framework becomes broadly accepted and well disseminated, and a cadre of well-trained analysts is built up to utilize it, available estimates are unlikely to be strictly comparable, meaning that the true opportunity costs of health sector resources invested in malaria control cannot be evaluated.

Conclusions

Malaria is a high priority for African policy-makers, who are faced with complex dilemmas over the design of prevention strategies, the selection of interventions to improve treatment, and the allocation of resources between malaria control and other health care problems. When considered in conjunction with information on affordability and feasibility, evidence from economic evaluations can assist policy-makers in identifying interventions representing the best value for money. Available studies provide some guidance to decision-makers. However, the current potential of economic evaluation to inform policy debates is limited by the gross lack of information on the costs and effects of many interventions, the very small number of CEAs available, the lack of evidence on the costs and effects of packages of measures, and the problems in generalizing or comparing studies that relate to specific settings and use different methodologies and outcome measures. The evidence base for ITNs has recently been greatly improved by the economic evaluations conducted alongside the main ITN trials. It is vital that all future trials of interventions also include economic components conforming to internationally accepted methodological standards, and that a much greater effort be made to assess costs and effectiveness of routine delivery of interventions.

References

Cost-effectiveness of malaria control measures


37 Greenwood BM. Bednets and mortality from malaria. Paper for the WHO Expert Committee on Malaria. London School of Hygiene and Tropical Medicine, 1998.


44 McCormick MC. The contribution of low birth weight to infant


**Acknowledgements**

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