

*Achieving the millennium development goals for health***Cost effectiveness analysis of strategies to combat malaria in developing countries**

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Abstract

Objective To determine the cost effectiveness of selected malaria control interventions in the context of reaching the millennium development goals for malaria.

Design Generalised cost effectiveness analysis.

Data sources Efficacy data came from the literature and authors' calculations supported by expert opinion. Quantities for resource inputs came from the literature and from expert opinion; prices came from the WHO-CHOICE database.

Methods Costs were assessed in year 2000 international dollars, and effects were assessed as disability adjusted life years averted by a 10 year implementation programme. Analysis was restricted to sub-Saharan regions where the most deadly form of malaria, *Plasmodium falciparum*, is most prevalent. The impact on population health for various interventions, and their combinations, was evaluated at selected coverage levels by using a state-transition model. Sensitivity analysis was done for age weights and discounting.

Results High coverage with artemisinin based combination treatments was found to be the most cost effective strategy for control of malaria in most countries in sub-Saharan Africa.

Conclusions A much larger infusion of resources than those currently available is needed to make headway in the fight to roll back malaria. On cost effectiveness grounds, in most areas in sub-Saharan Africa greater coverage with highly effective combination treatments should be the cornerstone of malaria control. However, treatment alone can achieve less than half the total benefit obtainable through a combination of interventions—and scaling up the use of impregnated mosquito nets or indoor spraying with insecticides is also critical. Intermittent presumptive treatment of pregnant women can bring a small but important additional health gain at relatively low cost.

Introduction

Each year, more than one million people die from malaria. The human toll is tragic, and the economic cost is enormous.^{1 2} Most of these deaths could be avoided, as effective and affordable ways to prevent and treat malaria exist. Malaria control is embedded in one of the millennium development goals of the United Nations: to “combat HIV/AIDS, malaria and other diseases.”³

Malaria related mortality seems to have increased since 1990, probably owing to a combination of factors, including increasing exposure to the disease,⁴ increasing resistance to antimalarial drugs,⁵ and stagnant levels of coverage with interventions. Achiev-

ing the millennium development goals requires a massive scaling up of interventions against malaria. We use a generalised cost effectiveness analysis to examine the costs and effects of scaling up seven interventions against malaria, allowing for interactions and consideration of whether current practice is optimal.

Methods**Geographical focus**

We focused on two sub-Saharan African regions: Afr-E (predominantly southern and eastern Africa) and Afr-D (predominantly western Africa). Table A on bmj.com gives a list of the countries by region. Both regions present large areas with endemic high transmission of malaria due to *Plasmodium falciparum*, although burden of disease differs. According to the World Health Report 2000, incidence of symptomatic malaria in children aged under 5 years was 1436 per thousand in Afr-D and 1184 per thousand in Afr-E. In Afr-E, cause specific child mortality is slightly higher at 8 per thousand compared with 7 per thousand in Afr-D.

Interventions

Preventive interventions, based on vector control, include insecticide treated bed nets and indoor residual spraying. Several drugs exist for treatment, and a few are relatively inexpensive. However, resistance to most drugs is growing rapidly. Combination treatments with and without artemisinin derivatives have been tested and found to be effective and to slow the growth of resistance.⁶ We evaluated seven individual interventions and combinations thereof (box 1). We did not consider complicated malaria needing admission to hospital.

Population at risk and coverage

We evaluated interventions at 50%, 80%, and 95% target coverage. We estimated effective coverage as target coverage multiplied by population at risk.⁷ We based region-wide estimates of population at risk (the proportion living in a malaria endemic area: 98% for Afr-D and 69% for Afr-E) on country specific figures (see bmj.com).⁷

Estimating the net effectiveness of interventions

We expressed the efficacy of bed nets and indoor spraying as a reduction in incidence and mortality, modelled through case fatality (see bmj.com). We estimated the net effectiveness of treatment, taking into account patients' behaviour (adherence to the regi-

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Extra tables and figures and an appendix are on bmj.com



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Costs, effectiveness, and cost effectiveness of the health maximising set of interventions (see table C on bmj.com for detailed results for all interventions)

Region and intervention	Average yearly costs (\$Int)	Average yearly effectiveness (DALYs averted)	Average cost effectiveness (\$Int/DALYs averted)	Incremental cost effectiveness (\$Int/DALYs averted)
Afr-D				
Case management with artemisinin based combination therapy (80% coverage)	72 386 626	7 771 018	9	9
Case management with artemisinin based combination therapy (95% coverage)	95 609 717	9 254 473	10	10
Insecticide treated bed nets plus case management with artemisinin based combination therapy plus intermittent presumptive treatment in pregnancy (95% coverage)	315 546 119	12 972 791	24	59
Indoor residual spraying plus insecticide treated bed nets plus case management with artemisinin based combination therapy plus intermittent presumptive treatment in pregnancy (95% coverage)	467 673 321	14 561 792	32	96
Afr-E				
Case management with artemisinin based combination therapy (95% coverage)	73 000 256	5 886 159	12	12
Insecticide treated bed nets plus case management with artemisinin based combination therapy (95% coverage)	254 755 715	9 138 452	28	56
Indoor residual spraying plus insecticide treated bed nets plus case management with artemisinin based combination therapy (95% coverage)	441 216 954	10 721 678	41	118
Indoor residual spraying plus insecticide treated bed nets plus case management with artemisinin based combination therapy plus intermittent presumptive treatment in pregnancy (95% coverage)	442 342 075	10 729 154	41	151

DALY=disability adjusted life year; \$Int=international dollar.

men), pharmacokinetics (probability of success when the regimen is not followed), and biogenetics (resistance of the parasite to the drug). These factors determine the number of expected treatment failures,⁸ which we subtracted from a common baseline of 98% efficacy (see bmj.com).

A population model⁹ combined estimates of incidence, prevalence, and mortality with estimates of prevalence and severity from the burden of disease study to project the population impact of intervention scenarios in terms of healthy years of life lived.¹⁰ Differences in total population healthy years under the intervention and baseline scenarios are expressed as disability adjusted life years (DALYs) averted.

Costs

Estimated costs are expressed in international dollars (\$Int, a hypothetical unit of currency that has the same purchasing power that the US\$ has in the United States at a given point in time, thus showing the average value of local currency units within each region's borders). We calculated costs in the light of experience from effectiveness trials, using data from the WHO-CHOICE database, primary data from several countries, existing literature, and expert

Box 1: Interventions evaluated

- Insecticide treated bed nets (ITN)
 - Indoor residual spraying (IRS)
 - Case management with chloroquine (CQ)
 - Case management with sulfadoxine-pyrimethamine (SP)
 - Case management with non-artemisinin based (CQ-SP) combination treatment (Comb)
 - Case management with artemisinin based combination treatment (ACT)
 - Intermittent presumptive treatment with SP in pregnancy (IPTp)
- (See appendix on bmj.com for details)

opinion.¹⁰ Cost calculations included unit cost of inputs, distribution, media campaigns, and labour costs (see bmj.com for details).

Results

Population level cost effectiveness estimates for individual and combined interventions are shown in the table (dominant interventions only) and in figures 1 and 2 (all interventions; figures A and B on bmj.com give more detail).

The “expansion paths” in the figures show the order in which interventions would be selected at different levels of resource availability. Notable differences exist between the regions. In Afr-D, case management with artemisinin based combination treatments at 80% target coverage is the most cost effective intervention overall and would be the first choice where resources are limited, whereas a target coverage of 95% is needed in Afr-E. In Afr-D, the second intervention on the path represents an increase in

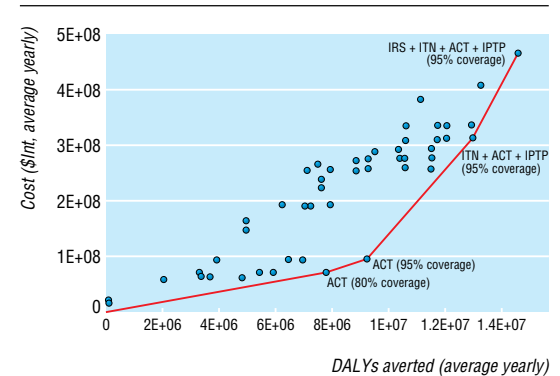


Fig 1 Cost effectiveness plane showing 60 analysed interventions (20 individual and combination interventions at three assumed coverage levels) and expansion path (see text), Afr-D. DALY=disability adjusted life year; see box 1 for other abbreviations

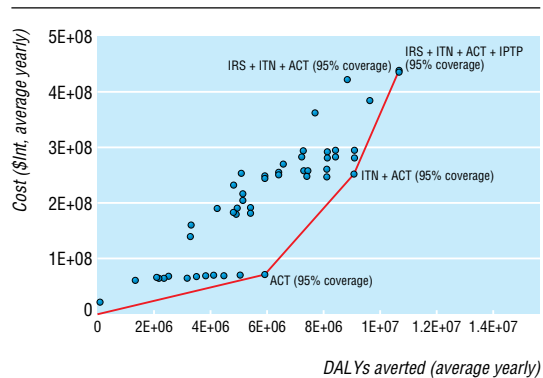


Fig 2 Cost effectiveness plane showing 60 analysed interventions (20 individual and combination interventions at three assumed coverage levels) and expansion path (see text), Afr-E. DALY=disability adjusted life year; see box 1 for other abbreviations

coverage with artemisinin based combination treatment. In both regions, however, use of insecticide treated bed nets (95% coverage) would be added after coverage with artemisinin based combination treatment reaches 95%, although in Afr-D intermittent presumptive treatment with sulfadoxine-pyrimethamine in pregnancy (95% coverage) would be added at the same stage. In both regions, the ultimate stage involves the use of case management with artemisinin based combination treatment, insecticide treated bed nets as well as indoor residual spraying, and intermittent presumptive treatment in pregnancy, all at 95% coverage.

All malaria interventions are highly cost effective, with average cost effectiveness ratios (except intermittent presumptive treatment with sulfadoxine-pyrimethamine in pregnancy) in the order of 10-100 \$Int/DALY averted. The size of potential health gains, as well as incremental cost effectiveness ratios, are more favourable in Afr-D than in Afr-E, as a higher proportion of the population is at risk in Afr-D (table).

Discussion

Principal findings

Box 2 shows the main messages from the analysis. To date, attention has been focused on drugs, other expendables, and additional staffing needed to scale up health interventions. This narrow focus ignores the additional system resources needed to implement and sustain a massive scale up of activity, as well as constraints on existing staff time and health facilities. Our results suggest that the costs of reaching agreed targets are considerably greater than the costs that receive most current attention.

Artemisinin based combination treatments are more expensive than other drugs, and, in the short term, non-artemisinin based combinations such as amodiaquine-sulfadoxine-pyrimethamine might be used as an interim measure.¹¹ However, as resistance to these drugs is increasing, recommendations should be guided by local resistance patterns,¹² and a full switch to artemisinin based combinations should be considered in all areas with high transmission of drug resistant *P falciparum* malaria.

Differences from other studies

This analysis differs from previous studies for malaria in that we have specifically assessed combinations of interventions, rather than assuming that costs and effects sum up when interventions are used concurrently.

In the only previous study analysing sub-Saharan Africa, Goodman et al found the cost/DALY averted of insecticide treated bed nets to be \$19-85 (US\$, 1995) compared with \$16-29 for indoor residual spraying.¹³ The estimates presented here (~30 \$Int/DALY for either intervention at 95% coverage in Afr-D and ~40 \$Int/DALY at 95% coverage in Afr-E) are roughly comparable. However, what does not emerge from typical cost effectiveness trials is the conclusion that implementing spraying and nets together has a cost effectiveness ratio roughly similar to that of either one alone (~35 \$Int/DALY at 95% coverage in Afr-D and ~48 \$Int/DALY at 95% coverage in Afr-E).

Limitations of the analysis

Our assumptions about the effectiveness of intermittent presumptive treatment with sulfadoxine-pyrimethamine in pregnancy were very conservative. We did not include health benefits for the mother, and the effect on the infant was limited to a reduction in case fatality due to malaria in the first year of life. Owing to lack of data on reductions in all cause mortality, we assumed that when drugs are taken under ideal conditions they are 98% effective in preventing cause specific mortality. Although we did try to account for parasite resistance, imperfect adherence to treatment, and pharmacokinetic properties, actual effectiveness is likely to include factors omitted in the analysis. Modelling implementation over a 10 year period, moreover, may not fully capture the contrast between drugs with high versus low growth rates of resistance (for example, sulfadoxine-pyrimethamine *v* artemisinin based combination treatment). Consequently, our estimate of the cost effectiveness of artemisinin based combination treatments may be conservative compared with when a longer term perspective is taken.¹⁴ Finally, the study allows no conclusions to be drawn about financing methods.¹⁵

Box 2: Main messages—malaria and the millennium development goals

- Five years on from the declaration of the millennium development goals, progress in controlling malaria remains uncertain, particularly in sub-Saharan Africa
- Health system decision makers in most countries in sub-Saharan Africa (see text for details) should consider switching treatment strategies to artemisinin based combinations as the foundation of effective malaria control
- Reinvigorating efforts to scale up use of impregnated mosquito nets and indoor spraying with insecticides is critical
- Where these interventions are being successfully implemented, intermittent presumptive treatment of pregnant women can bring a small but important additional health gain
- A much larger infusion of resources than those currently available is needed to make headway in the fight to roll back malaria

What is already known on this topic

Insufficient data are available to fully assess global malaria trends since 2000, but malaria related mortality seems to have increased since 1990

Despite the existence of effective preventive and curative strategies, current malaria control in sub-Saharan Africa remains poor

Achieving the malaria specific millennium development goal requires a massive scaling up of interventions in sub-Saharan Africa

What this study adds

This study quantifies the advantages of shifting resources towards artemisinin based combination treatment, as well as of using preventive and curative interventions in combination

A much larger infusion of resources than those currently available, and more attention to health system strengthening, is needed to make headway in the fight to roll back malaria

Implications of the study

In conclusion, with the availability of increased international funding, a re-evaluation of existing and potential strategies is appropriate. An adequate portion of new funds should be allocated to strengthening the health system components of malaria interventions, which will determine the long term viability of these activities.

On purely cost effectiveness grounds, this study suggests that most countries in sub-Saharan Africa should be moving to combination therapy with new drugs and that efforts should be regenerated to ensure that interventions based on prevention, such as nets and spraying, are scaled up appropriately.

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One hundred years ago

Nelson's personal experiences of surgery

Nelson was a man of weak frame and of a constitution which in these days would be called neurotic. This makes his physical courage and the vigorous vitality which enabled him to bear the rough life of the navy as it was in his day all the more remarkable. While he was still a midshipman the Indian climate broke down his health for a time. Southey says: "The disease baffled all power of medicine; he was reduced almost to a skeleton; the use of his limbs was for some time almost entirely lost." He was brought home, and had it not been for the care of a kindly captain he would never have lived to reach his native shores. So depressed was he at this time that he almost despaired of ever rising in his profession. He says himself: "After a long and gloomy reverie, in which I almost wished myself overboard, a sudden glow of patriotism was kindled within me, and presented my king and country as my patron. 'Well, then,' I exclaimed, 'I will be a hero! and confiding in Providence, I will brave every danger.'" Later in the West Indies he suffered

from poisoning from drinking at a spring into which some boughs of the machineel had been thrown. The effects were so severe as, in the opinion of some of his friends, to inflict a lasting injury on his constitution. Not long afterwards he suffered from dysentery, which reduced him so much that when the expedition reached Port Royal he was carried ashore in his cot. He was again invalided home. He went to Bath in a miserable state—so helpless that he had to be carried to and from his bed, and the act of moving him caused the most violent pain. Before his health was thoroughly re-established he was sent to the North Seas and kept there a whole winter, as if, he said, to try his constitution. Throughout his life he had often to contend with ill health, and he never went to sea without suffering from sickness for the first few days—a fact which of itself testifies to his indomitable spirit as much as his heroic exploits.

(*BMJ* 1905;ii:1067)