Research

Cost-effectiveness of iron supplementation and malaria chemoprophylaxis in the prevention of anaemia and malaria among Tanzanian infants

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Prerequisites for effective interventions against severe anaemia and malaria among infants are economic evaluations to aid the setting of priorities and the making of health policy. In the present study we analysed the cost and effectiveness of three control strategies hypothetically delivered through the Expanded Programme on Immunization (EPI). For the prevention of severe anaemia and from the perspective of the health provider, the cost-effectiveness ratios were, respectively, US$ 8, US$ 9, and US$ 21 per disability-adjusted life year (DALY) for malaria chemoprophylaxis with Deltaprim (a combination of 3.125 mg pyrimethamine and 25 mg dapsone) + iron, Deltaprim alone, or iron supplementation alone. For malaria prevention, Deltaprim + iron cost US$ 9.7 per DALY and Deltaprim alone cost US$ 10.2 per DALY. From a sociocultural perspective the cost-effectiveness ratios ranged from US$ 9 to US$ 26 for severe anaemia prevention and from US$ 11 to US$ 12 for the prevention of clinical malaria. These ratios were highly cost-effective, as defined by the World Bank's proposed threshold of less than US$ 25 per DALY for comparative assessments. Furthermore, all the preventive interventions were less costly than the current malaria and anaemia control strategies that rely on clinical case management. This economic analysis supports the inclusion of both malaria chemoprophylaxis and iron supplementation delivered through EPI as part of the control strategies for these major killers of infants in parts of sub-Saharan Africa.

Keywords: anaemia; antimalarials; cost–benefit analysis; health care costs; iron-deficiency; malaria; United Republic of Tanzania.

Voir page 105 le résumé en français. En la página 105 figura un resumen en español.

Introduction

Malaria is responsible for 4% of global deaths (*1*). Sub-Saharan Africa suffers most of the burden of mortality and morbidity from malaria, accounting for over 85% of the disability-adjusted life years (DALYs) attributable to the disease (*2*). Over half the children in developing countries suffer from anaemia (*3*), with malaria and iron deficiency being the main etiological factors. Severe anaemia and malaria are also a significant burden on health facilities in sub-Saharan Africa, accounting for much of the hospitalization and use of external health services (*4, 5*). Malaria control in Africa continues to rely on the adequate and prompt treatment of suspected cases (*6*). Primary prevention by means of prophylactic drugs or vector control is rare. Interruption of contact between humans and vectors through the use of insecticide-treated bednets is a promising approach that is slowly being implemented. The reduction of iron-deficiency anaemia is one of the goals of WHO and UNICEF (*7*); however, despite recommendations to provide routine oral iron supplementation for pregnant women and young children, targeted programmes for children are rarely implemented in developing countries.

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The economic appraisal of health interventions is vital for guiding the formulation of health policies, particularly because of the limited resources of the health sector, the growing complexities of health systems, and the poor performance of most national economies in sub-Saharan Africa. Economic analysis involves reliable assessment of the epidemiology and burden of disease as well as the acquisition of information on the cost and effectiveness of strategies for health improvement (*8*). In 1995 it was estimated that the economic impact of malaria in Africa could rise to US$ 1.7 billion (1700 million) (*9*). In sub-Saharan Africa, several studies have established the cost-effectiveness of control strategies such as the use of impregnated bednets and chemoprophylaxis in children under 5 years of age (*10*). However, at the population level targeted interventions for malaria and anaemia control among infants (i.e. under 1 year of age) have not been sufficiently assessed from the economic standpoint.

A recent randomized controlled clinical trial showed that, in an area of intense perennial malaria transmission, malaria chemoprophylaxis and/or iron supplementation were safe and efficacious in preventing both severe anaemia and clinical malaria episodes in infants aged under 1 year (*4*). On the basis of this study, we report in this paper the cost-effectiveness of these control strategies, within the structural setting of the Expanded Programme on Immunization (EPI) in Kilombero District, United Republic of Tanzania, taking into consideration the health care provider's perspective and the socio-cultural circumstances. The costs of these interventions are compared with those of standard case management and, in terms of the hypothetical effectiveness of the latter, the cost-effectiveness ratios of standard case management are evaluated and contrasted with the most cost-effective primary prevention strategy.

Materials and methods

Study area and population

The study was conducted in Kilombero District (population in 1996: ca. 187 900), United Republic of Tanzania. The characteristics of the area and its health care system have been described elsewhere (*11*). Most villagers are subsistence farmers, growing rice, maize and cassava, and there is an increasing number of small traders. The houses mainly have thatched roofs and mud walls; water supplies and waste disposal are often inadequate. Government health facilities include the Saint Francis Designated District Hospital, a mother and child health clinic, two health centres, and thirteen dispensaries; in addition there are some private health centres. There is a high perennial rate of transmission of *Plasmodium falciparum* malaria, one of the principal causes of child morbidity and mortality. The study's target population comprised infants (i.e. under-1- year-olds) living in Kilombero District, which is also the hospital-coverage infant population; in 1996 there were approximately 2322 under-1-year-olds in the area.

Intervention strategies and effectiveness data

Efficacy data were obtained from the randomized placebo-controlled clinical trial. The three strategies employed were based on the use of preventive drugs to complement routine case management of new cases, as summarized below.

- Daily iron supplementation (iron(II) sulfate syrup in drops containing 25 mg iron per 5 ml) administered by mothers to infants from 2 months to 6 months of age; the target daily dose of iron was 2 mg/kg body weight.
- Weekly malaria chemoprophylaxis with a combination of 3.125 mg pyrimethamine and 25 mg dapsone per 5 ml (Deltaprim) administered at home by village health workers to infants from 2 months to 12 months of age at a dose of 2.5 ml per week.
- A combination of the two previous interventions, i.e. iron supplementation plus malaria chemoprophylaxis (Deltaprim).

Cases were ascertained through passive detection as well as cross-sectional surveys of infants aged 8–52 weeks. An episode of severe anaemia was defined as a packed cell volume <25%; and a clinical episode of malaria, on the basis of an axillary temperature $\geqslant 37.5\ ^{\circ}C$ and the presence of asexual *P. falciparum* parasites at any density.

For the economic analysis we used efficacy estimates derived from an "intention to treat" analysis. Included, therefore, were both compliant and noncompliant subjects from the randomized clinical trial. Compliance with the intervention drugs during the trial was estimated to be above 70%. Incidence estimates obtained from the placebo group were 0.62 episodes per person-year and 0.71 episodes per person-year for severe anaemia and first clinical malaria episodes, respectively (*4*).

It was assumed that the interventions were delivered through EPI in the mother and child health programme, and two contacts with the health services were considered, coinciding with second and third diphtheria–tetanus–pertussis and poliovirus immunizations when the infants were aged 2 months and 3 months, respectively. The mothers administered both iron and chemoprophylaxis at home as stipulated above. The first contact was for training the mothers on the mode of drug administration, while the second was for retraining and the issuing of new prepackaged drugs.

Each strategy's effectiveness was expressed as years of life lost (YLLs) and DALYs, discounted at 3% (*12*). The result of the effectiveness of the interventions is thus the number of DALYs saved with each preventive strategy, i.e. subtraction of the burden of disease with intervention from the burden without intervention.

DALYs were obtained by adding YLLs and years lived with disability (YLDs). The calculation included YLLs expressed as the difference between age at death and life expectancy for each age, further modified by age weighting. Life expectancy for each age was assigned for females from Model Life Table West 26 (*13*) and for males from Model Life Table West 25 (*14*).

The number of deaths was estimated from the incidence of severe anaemia or first clinical malaria episodes and the case fatality rate. Disability weights were assigned on the basis of those used in a previous study (*3*). We assumed that surviving cases had no sequelae. Estimates of case fatality rates were obtained from a prospective cohort of hospitalized children in the same area: the mean values were 6.1% for severe anaemia and 4.7% for hospitalized cases of malaria episodes. By reference to the literature and expert opinion, the mean durations of episodes of treated severe anaemia and of malaria were determined as 3 months and 28 days, respectively.

Cost measurements

Cost-effectiveness ratios were expressed as cost in US$ (1996 values) per unit of outcome achieved (expressed as DALYs averted). The incremental cost-effectiveness (i.e. the ratio of the differences between costs (C) over the difference between effectiveness (E): $(C_a - C_b)/(E_a - E_b)$ was estimated when one intervention was more expensive and more effective than another. The comparisons related to the costs for health care providers only and separately to those for families.

Estimates for preventive interventions included the costs of preventive intervention for health care providers (a), plus the treatment costs of severe anaemia and malaria episodes (not prevented) for the health care providers (b), plus the household costs of treating severe anaemia and malaria episodes (not prevented) for families (c) (direct and indirect costs).

The cost assessment for standard case management comprised the treatment costs of severe anaemia and malaria episodes for the health care provider (b), plus the household costs (direct and indirect costs) of treating severe anaemia and malaria episodes for families (c), as discussed below.

(a) Costs of intervention in coverage population for health care providers. The costs of each intervention were calculated from the respective unit prices and the total quantities of goods and services needed. The information on costs was generated from the detailed project files on cost accounting available at the Saint Francis Designated District Hospital, the Fundació Clinic Administration Office, UNICEF and Zimbabwe Pharmaceuticals (supplier of Deltaprim). Quantities, goods and price estimates were obtained from a previous study (*4*). All costs were converted to US$ at the mid-1996 exchange rate (580 Tanzanian shillings = US$ 1). A one-year period was used for costs. A 2% discount was applied to costs not directly available for 1996, such as those for drugs carrying 1998 prices. The capital costs of training, which was assumed to last two years, were annualized, but those of items such as buildings, which the interventions made little use of, were not included (*15*).

Personnel costs were obtained from the true 1996 salaries paid at the Saint Francis Designated District Hospital and the mother and child health clinic; they included crude salaries, taxes and insurance for workers. We estimated that 25% of a supervisor's time was used in implementing, coordinating, and supervising the preventive intervention. It was assumed that health workers could dedicate their daily working hours to instruction and to give medication to a maximum of 50 mother and child pairs. The costs of drugs included insurance, travel and wastage; costs of preventive intervention for families, such as travel or days of work lost, were not taken into consideration because they were covered by customary EPI visits.

(b) Treatment costs of severe anaemia and malaria episodes for health care providers. The data are based on activity at the Saint Francis Designated District Hospital in 1996 (*16, 17*). The number of cases needing treatment for severe anaemia or clinical malaria varied with the effectiveness of each intervention in reducing the incidence of each disease. Costs were based on the treatment of 100% of the cases of disease, although many persons did not seek treatment from the formal health system. The cost of treatment was the weighted average of the costs of case management. The annex shows details of the calculation of the cost of management of cases of anaemia and malaria.

Standard severe anaemia treatment included the administration of iron(II) sulfate tablets, folic acid and chloroquine, and, in some cases, blood transfusion. Additional treatments required to deal with complications related to severe anaemia, such as congestive heart failure, were not included, since the incidence of complications was unknown and it was assumed that costs did not rise substantially. The case management of a clinical malaria episode in a child under the age of 1 year included the administration of chloroquine and/or quinine and Fansidar (sulfadoxine + pyrimethamine) in different regimens, depending on the clinical presentation. Costing did not take account of resistance to antimalarials.

(c) Household costs of treatment of severe anaemia and malaria episodes. The direct and indirect costs of treating malaria and anaemia in infants were studied by means of a specific questionnaire administered to 618 mothers of children with clinical diagnosis of these conditions (*18*). Intangible costs, such as the monetary value of pain and suffering for the patient and the patient's family, were not included. The cost of time lost was calculated on the basis of the minimum Tanzanian wage of 17 500 Tanzanian shillings (approximately US$ 30) per month.

Sensitivity analysis

Univariate sensitivity analysis was based on the effectiveness estimate derived from the lower 95% confidence interval limit for efficacy, further adjusted for the drop in compliance at the second visit. Attendance in connection with the second scheduled EPI visit was estimated to be 80% (*19*). Changes in the percentages of cases of severe anaemia and clinical malaria treated in accordance with standard case management were also tested.

Bivariate analysis (two-way sensitivity analysis) was performed, the hypothesized effectiveness of the standard case management strategy and the cost of case treatment being taken as independent variables. The range of the tested effectiveness estimates was from the lowest possible (0%) to the highest possible gain in health (95% effectiveness), according to the known burden of severe anaemia or clinical malaria in infants. For this analysis the cost-effectiveness ratios of D + I (Deltaprim + iron) and standard case management were made equal to obtain the iso-cost-effectiveness curve (i.e. a set of points depending on the previous variables at which both cost-effectiveness ratios were the same). This curve separates two areas in which one of the two strategies is more cost-effective (see Fig. 1).

The data were processed using Microsoft Excel for Windows, version 7.0 and SAS software.

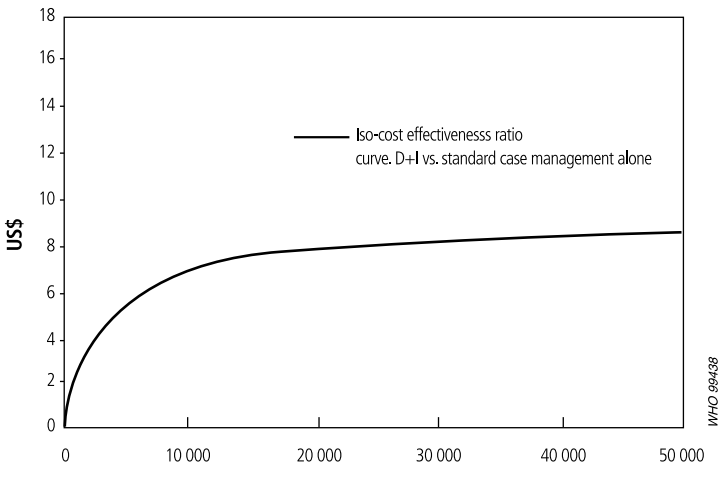
Results

The cost menu for the interventions is presented in Table 1. The costs to the health provider for the management of cases of severe anaemia and clinical malaria episodes in infants amounted to US$ 16.3 and US$ 14.6 per episode, respectively (see annex). Household costs per episode of severe anaemia or clinical malaria amounted to US$ 4.5, the principal components being indirect. Based on previously available data, Table 2 shows the costs of standard case management and of the three different intervention strategies for the prevention of severe anaemia and clinical malaria in the reference population. For the management of both severe anaemia and clinical malaria episodes, all preventive interventions had lower cost estimates than the approach based on standard case management alone. Treatment with Deltaprim alone generally yielded the lowest costs.

The effectiveness estimates for the different interventions for the evaluation of the prevention of severe anaemia and first clinical malaria episodes (i.e. keeping a child free of clinical malaria during her/his first year of life) are shown in Table 3. Deltaprim + iron was the most effective strategy for all effectiveness estimate assumptions.

The resultant cost-effectiveness ratios and marginal cost-effectiveness ratios are given in Table 4. The most cost-effective intervention for the prevention of both severe anaemia and clinical malaria was that involving the administration of Deltaprim + iron.

Fig. 1. **Iso-cost-effectiveness ratio curve for treatment alone and preventive strategies, depending on weighted cost of severe anaemia treatment and effectiveness of standard case management.** (The iso-cost-effectiveness curve separates two areas where we would choose one strategy over another since it would be more cost effective. If the cost and effectiveness of standard case management lies in the area above the curve, we would choose D+I.)



Sensitivity analysis

In the scenario of a low-effectiveness estimate the cost-effectiveness ratios increased, especially those relating to iron supplementation alone. Deltaprim + iron supplementation continued to be the most cost-effective intervention (Table 5).

With regard to the varying percentages of episodes treated through the health care system, sensitivity analysis of the cost-effectiveness ratios showed that at the lower levels of cases treated the costs and cost-effectiveness ratios decreased for all interventions (Fig. 2). Because of variations in health care costs, the cost-effectiveness ratios were very sensitive to the number of cases of disease treated in the health care system. From the standpoint of the health care provider, use of Deltaprim + iron was the most cost-effective strategy for both severe anaemia and malaria, with 40% and 60% of cases treated, respectively (Fig. 2a, b). From the socio-cultural standpoint the cost of standard case management alone was higher than the costs of all other interventions when the number of cases treated by the health care system was greater than 30% (Fig. 2c, d).

The results of the two-way sensitivity analysis, comparing the cost-effectiveness of Deltaprim + iron and standard case management are illustrated in Fig. 1 and Fig. 3. The costs of managing cases of severe anaemia and clinical malaria episodes, US$ 8.5 and US$ 8, respectively, lie in the area above the curve. From the cost-effectiveness standpoint this

Table 1. **Cost menu for economic analysis of intervention strategies**

	Units	Unitary value (in 1996 US$)	Observations
Recurrent costs			
Iron[a]	US$ per full course anaemia prevention intervention	1.01	Yearly inflation rate considered to be 2%.
Deltaprim[b]	US$ per full course anaemia and malaria prevention intervention	2.00	Price originally given in Zimbabwean dollars. Exchange rate was mean 1995–96 rate: US$ 1 = Zimbabwean $ 9.01
Health worker[c]	US$ per month	60.34	100% of worker's time is required. With 20 working days per month, cost per working day is US$ 3
Supervisor[c]	US$ per month	63.80	25% of supervisor's time required. Cost per working day is US$ 0.8.
Driver[c]	US$ per week	10.00	1 week per year is required.
Stationery[c]	US$ per treatment	0.25	
Vehicle hire + running costs[c]	US$ per year	259.00	With 3-year life and 8% time for this programme.
Capital costs			
Trainer[c]	US$ per training session	7.97	Training for 1 week required. Effects of training assumed to last for 2 years. Costs were annualized.

[a] Source: UNICEF's January 1998 price.

[b] Source: Zimbabwe Pharmaceuticals, Harare, Zimbabwe.

[c] Source: District Health Office, Ifakara, Tanzania.

Table 2. **Costs of case management and of three different intervention strategies for the prevention of severe anaemia and clinical malaria in the reference population of 2322 infants in Kilombero District, United Republic of Tanzania (in US$, 1996 values)**

	Control	Intervention		
	Standard case management	Deltaprim + iron	Delta-prim	Iron
Severe anaemia				
A. Cost of intervention	0	8 772	6 424	4 121
B. Cost of anaemia treatment	23 600	7 439	9 485	16 022
C. Direct household costs of anaemia treatment	768	243	309	521
D. Indirect household costs of anaemia treatment	5 796	1 827	2 329	3 935
Total cost for health care provider (A+B)	23 600	16 211	15 909	20 143
Total cost for health care provider and households (A+B+C+D)	30 164	18 280	18 547	24 600
Cost per child for health care provider	10.2	7.0	7.0	9.0
First episode of clinical malaria				
A. Cost of intervention	0	8 772	6 424	—
B. Cost of clinical malaria treatment	24 152	8 226	9 806	—
C. Direct household cost of clinical malaria episode treatment	876	298	356	—
D. Indirect household cost of clinical malaria episode treatment	6 611	2 252	2 684	—
Total cost for health care provider (A+B)	24 152	16 998	16 229	—
Total cost for health care provider and households (A+B+C+D)	31 638	19 548	19 269	—
Cost per child for health care provider	10.4	7.3	7.0	—

Table 3. **Effectiveness estimates[a] and DALYs saved for three intervention strategies for prevention of severe anaemia and first clinical malaria episodes related to standard case management (in US$, 1996 values)**

	Standard case management	Deltaprim + iron	Deltaprim	Iron
Severe anaemia				
Effectiveness estimate[b]		68.5%	59.8%	32.1%
Burden of disease (DALYs)[d]	2999	945	1205	2036
Years of life saved[d]		2040	1782	957
DALYs saved[d]		2054	1794	963
Low effectiveness estimate[c]		52.3%	41.1%	4.6%
Burden of disease[e]	2999	1744	2013	2889
Years of life saved[e]		1246	979	110
DALYs saved[e]		1255	986	110
First episodes of clinical malaria				
Effectiveness estimate[b]		65.9%	59.4%	
Burden of disease (DALYs)[d]	2668	909	1083	
Years of life saved[d]		1755	1581	
DALYs saved[d]		1759	1585	
Low effectiveness estimate[c]		39.7%	32.9%	
Burden of disease[e]	2668	1605	1791	
Years of life saved[e]		1060	875	
DALYs saved[e]		1063	877	

[a] Effectiveness estimates correspond to the percentage reductions in the incidence of severe anaemia or clinical malaria with regard to the control group (*4*).

[b] Relates to the ''intention to treat'' efficacy estimate obtained in the randomized clinical trial.

[c] Relates to the lower 95% confidence interval of the efficacy estimate further adjusted for 20% loss in attendance at second visit.

[d] Related to the effectiveness estimate.

[e] Related to the low effectiveness estimate.

favours the preventive approach over the standard case management strategy.

Discussion

The three intervention strategies for the prevention of severe anaemia and malaria in infants appear to be highly cost-effective, with the combination Deltaprim + iron being the most cost-effective. Even though cost-effectiveness ratios are very sensitive to low effectiveness estimates, those for Deltaprim + iron remain within the limits of high cost-effectiveness (<US$ 25 per DALY). The costs for all intervention strategies (taking into account the management costs for cases not prevented through the new strategies) are lower than the costs for control through standard case management alone. Although health-seeking behaviour influences costs and cost-effectiveness ratios, the alternative intervention strategies are nevertheless more favourable from a cost-saving or cost-effectiveness standpoint than the present strategy. Furthermore, if the cost of managing a case is >US$ 8 for malaria and >US$ 8.5 for severe anaemia (at any level of effectiveness of standard case management), the Deltaprim + iron treatment is always more cost-effective than clinical case management alone.

Basically, the framework of cost-effectiveness analysis uses a microanalysis perspective without taking into account the impact on other sectors of society. Whereas most evaluations of preventive interventions fail to include some of the costs of routine case management for the health provider (*20, 21*), our study includes this important element. Nonetheless, caution should be adopted in deriving public health policy solely from what remains a microeconomic analysis.

The use of DALYs to measure outcome enables comparison with interventions targeted at different population groups or diseases. This is also an equitable approach to the burden of disease in developing countries with relatively low life expectancies (*12*). The problems encountered in determining disease burden include the following:

– the uncertainty inherent in assessing disability in infants;
– the contribution that malaria and/or anaemia may make to morbidity and mortality;
– competing risks that may lower the burden attributable to these diseases;
– problems involved in measuring effectiveness.

With regard to the last of these problems, we encountered two major difficulties. The first concerns the relatively arbitrary decision on the duration of follow-up from which effectiveness estimates should be derived. The second has to do with the use of hospital-derived case fatality rates to estimate mortality in instances when the size of the study from which the efficacy estimates are taken is too small to include mortality as a main outcome. The burden of disease and its limitations are important factors to consider when assessing the relevance of cost-effectiveness ratios.

The results of the present study are not readily comparable with those of other malaria control trials in Africa. In the Gambia, the cost-effectiveness of insecticide-treated bednets in 1990 was US$ 188 per death averted (*21*); the addition of chemoprophylaxis increased the cost to US$ 257 per death averted. Malaria chemoprophylaxis alone was estimated to cost US$ 143 per death averted (*10*). The framework used for the analysis of these trials did not include the costs of clinical case management, and the outcome measurements differ. Nevertheless, with a comparable outcome measurement such as the cost per child-year protected, the previous interventions present a similar range of costs to that reported here. Malaria control with insecticide-treated bednets cost US$ 5.6 per child-year protected, and combined with chemoprophylaxis increased to US$ 7.5 per child-year protected. Malaria chemoprophylaxis alone was estimated to cost US$ 2.8 per child protected per season. In our study the cost per child-year protected was US$ 7–9 at 1996 values.

Compared with other major public health interventions the malaria and anaemia control strategies reported in this paper also performed favourably. Vitamin A supplementation and childhood immunization by EPI cost US$ 12 and US$ 17 per DALY, respectively (*22*). Both these interventions, as well as the malaria and anaemia control strategies, have cost-effectiveness ratios in the range of those prioritized and qualified as highly attractive for developing countries by the World Bank (*22*). These strategies should perform similarly in other areas where the malaria morbidity load, transmission and health system structure are analogous to those in Kilombero District.

In view of the available estimates of malaria morbidity and mortality throughout sub-Saharan Africa, it is easy to conclude that current malaria control strategies are grossly unsatisfactory. Control continues to rely on the prompt treatment of suspected cases. The sole preventive tool, the insecticide-treated bednet, is only being introduced slowly through social marketing schemes. It is regarded as a personal protection measure for which the individual has to pay, and not as a major public health intervention to be supported by national policy and budgets. The use of drugs in malaria control has been further limited by the development and spread of resistance to chloroquine and Fansidar. This is a clear drawback to chemoprophylaxis for the control of malaria among infants. Further work is required to determine the contribution that a targeted prophylaxis programme for such children might make to the development and spread of resistance, and the dosage at which the development of naturally acquired clinical immunity would not be impaired. These considerations do not apply to iron supplementation, which has been shown to be safe and efficacious in preventing anaemia at the dosage used in this study, without increasing the risk of malaria.

In the United Republic of Tanzania, the combination of malaria chemoprophylaxis and iron supplementation is cost-effective and cost-saving. There is an urgent need for improved, evidence-based and economically sound malaria control throughout the whole of Africa. The results reported in the present paper favour the inclusion of both malaria chemoprophylaxis and iron supplementation delivered through EPI as a means of improving the control of malaria and anaemia, two major killers of infants in parts of sub-Saharan Africa. ■

Table 4. **Cost-effectiveness (C/E) ratios for prevention of severe anaemia and first clinical malaria episodes (in US$, 1996 values), and marginal cost-effectiveness ratios for Deltaprim + iron**

	Delta-prim + iron	Delta-prim	Iron
Severe anaemia			
C/E ratio (US$ per DALY averted)			
Health care provider perspective	7.9	8.9	20.9
Sociocultural perspective[a]	8.9	10.3	25.5
Marginal C/E ratio[b] (Health care provider perspective)	1.2		
Marginal C/E ratio[c] (Health care provider perspective)	14.9		
First episodes of clinical malaria			
C/E ratio (US$ per DALY averted)			
Health care provider perspective	9.7	10.2	
Sociocultural perspective[a]	11.1	12.2	
Marginal C/E ratio[b] (Health care provider perspective)	4.4		

[a] Health care provider and households (direct and indirect costs).

[b] Due to higher costs of Deltaprim + iron intervention, marginal cost-effectiveness ratio is calculated as the base value: Deltaprim.

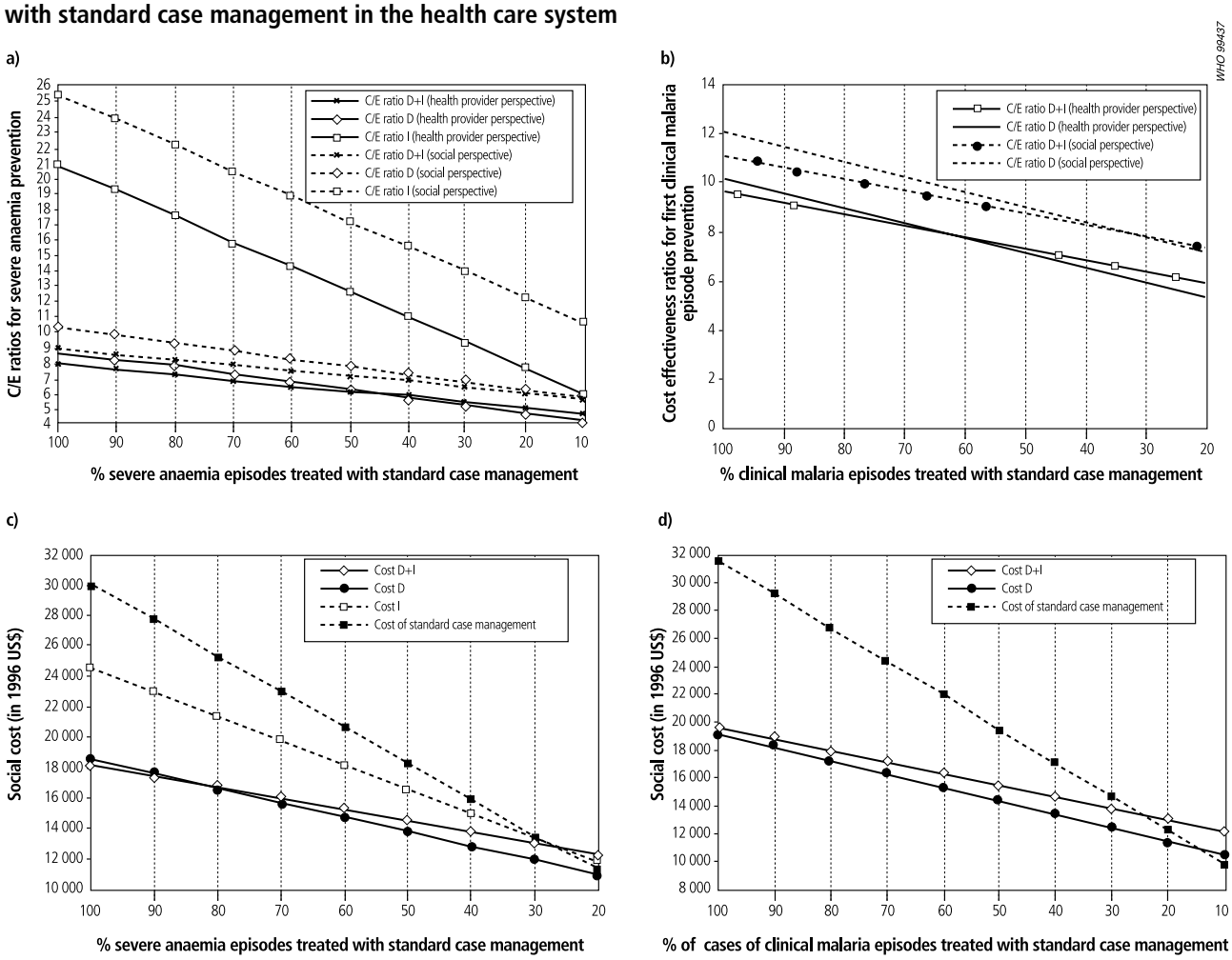
[c] Marginal cost-effectiveness ratio is calculated as the base comparative value: iron.

Table 5. **Costs and cost-effectiveness (C/E) ratios for the prevention of severe anaemia and first clinical malaria episode using a low effectiveness estimate (in US$, 1996 values)**

	Standard case management	Delta-prim + iron	Delta-prim	Iron
Severe anaemia				
Total cost for health care provider	23 600	22 498	22 264	26 853
Total cost for health care provider and households	30 164	26 315	26 670	33 175
Cost-effectiveness ratios				
Health care provider perspective		17.9	22.6	243.3
Sociocultural perspective[a]		20.9	27.0	300.6
First episodes of clinical malaria				
Total cost for health care provider	24 152	23 304	22 634	
Total cost for health care provider and households	31 639	27 809	27 659	
Cost-effectiveness ratios				
Health care provider perspective		21.9	25.8	
Sociocultural perspective[a]		26.2	31.5	

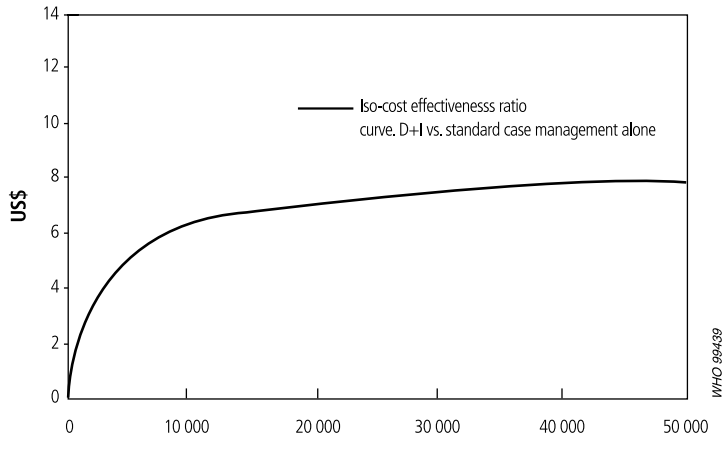
[a] Health care provider and households (direct and indirect costs).

Fig. 2a–d. **Sensitivity analysis of cost-effectiveness ratios (C/E) and costs, according to the percentage of cases treated with standard case management in the health care system**



D+I = deltaprim and iron supplementation intervention strategy; D = deltaprim alone intervention strategy; I = iron supplementation alone intervention strategy

Fig. 3. **Iso-cost-effectiveness ratio curve for standard case management alone and preventive strategies, depending on weighted cost of clinical malaria treatment and effectiveness of standard case management.** (The iso-cost-effectiveness curve separates two areas where we would choose one strategy over another since it would be more cost effective. If the cost and effectiveness of standard case management lies in the area above the curve, we would choose D+I.)



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Résumé

Rapport coût/efficacité de l'administration de suppléments de fer et de la chimioprophylaxie du paludisme pour la prévention de l'anémie et du paludisme parmi des nourrissons tanzaniens

Pour orienter les politiques de santé de façon rationnelle, surtout au moment même où le coût des soins est un sujet de préoccupation croissante, il faut pouvoir évaluer avec fiabilité l'épidémiologie des maladies et la charge qu'elles représentent de même que rassembler des données sur le coût et l'efficacité des stratégies d'amélioration de la santé. Le paludisme et l'anémie comptent parmi les grandes menaces pour la vie des jeunes enfants en Afrique subsaharienne. Les stratégies de lutte actuelles se fondent sur la prise en charge rapide des cas cliniques dans les établissements de santé. A partir des résultats sur l'efficacité obtenus dans le cadre d'un essai clinique randomisé contre placebo, nous avons procédé à une analyse économique et comparé le rapport coût/efficacité de trois stratégies différentes de lutte contre le paludisme et l'anémie sévère chez les nourrissons du district de Kilombero, une zone de la République-Unie de Tanzanie où la transmission du paludisme est constante. On a comparé les coûts de la stratégie de lutte actuellement appliquée, qui repose uniquement sur la prise en charge standard des cas, avec ceux des interventions ci-après :

– administration quotidienne de suppléments de fer (F) ;
– chimioprophylaxie hebdomadaire du paludisme avec le Deltaprim (association de 3,125 mg de pyriméthamine et 25 mg de dapsone) (D) ; et
– association des deux traitements ci-dessus (D+F).

L'analyse économique a été effectuée dans le cadre hypothétique des interventions du Programme élargi de Vaccination (PEV). Les estimations de coûts portaient, d'un côté, sur chaque intervention dans la population visée du point de vue du prestateur de soins et, de l'autre, sur le traitement des cas non évités, en même temps que sur les coûts pour les ménages du traitement des cas non évités. L'évaluation de coûts pour la stratégie de lutte actuelle fondée sur la prise en charge standard des cas correspondait à la somme du coût de la prise en charge des cas (pour le prestateur de soins) et des coûts pour les ménages du traitement des cas (coûts directs et indirects). Du point de vue du prestateur de soins, les rapports coût/efficacité pour la prévention de l'anémie sévère étaient les suivants : US $7,9 par année de vie corrigée du facteur invalidité (AVCI) pour D + F, US $8,9 par AVCI pour D, et US $21,0 par AVCI pour F. Du point de vue socioculturel (y compris également les coûts pour les familles), les rapports coût/efficacité allaient de US $9 par AVCI pour D + F à US $26 par AVCI pour F. Pour la prévention des accès de paludisme clinique durant la première année de la vie, les rapports coût/efficacité étaient de US $9,7 et US $10,2 par AVCI pour les stratégies D + F et D, respectivement. Dans une perspective socioculturelle, on a obtenu des rapports coût/efficacité de US $11 et US $12 par AVCI pour D + F et D, respectivement. Toutes les interventions préventives étaient génératrices d'économies par rapport à la stratégie de lutte fondée uniquement sur la prise en charge standard des cas, mais l'intervention conjuguant administration de suppléments de fer et chimioprophylaxie du paludisme était la plus efficace et la plus rentable. Si le coût de la prise en charge des cas dépassait US $8,5 pour l'anémie sévère et US $8 pour les accès de paludisme clinique, D + F était plus rentable que la prise en charge standard des cas à tous les niveaux d'efficacité de cette dernière intervention. L'utilisation d'antipaludiques associée à l'administration de suppléments de fer parmi les nourrissons est une formule d'un très bon rapport coût/efficacité pour les pays où le mode de transmission du paludisme et la structure du système de santé sont comparables à ceux du district de Kilombero, en République-Unie de Tanzanie. Cette analyse économique confirme qu'il est justifié d'inscrire dans les stratégies de lutte contre le paludisme et l'anémie tant la chimioprophylaxie que l'administration de suppléments de fer dans le cadre du PEV.

Resumen

Relación costo-eficacia de los suplementos de hierro y la quimioprofilaxis antipalúdica en la prevención de la anemia y el paludismo entre los lactantes de Tanzanía

Para dirigir políticas de salud racionales, sobre todo en una época de creciente preocupación por el gasto sanitario, es necesario disponer de una evaluación fidedigna de la epidemiología y la carga de morbilidad, así como de información sobre el costo y la eficacia de las estrategias de mejora de la salud. El paludismo y la anemia matan a muchos niños pequeños en el África subsahariana. Las actuales estrategias de control dependen de un pronto manejo de los casos clínicos en los servicios de salud. A partir de los resultados de eficacia obtenidos en un ensayo clínico aleatorizado controlado mediante placebo, llevamos a cabo un análisis económico y comparamos la eficacia en función de los costos de tres estrategias de control del paludismo y de la anemia grave entre lactantes del distrito de Kilombero, una zona de la República Unida de Tanzanía donde la transmisión del paludismo tiene carácter perenne. Se procedió a comparar el costo de la actual estrategia de control, basada únicamente en el manejo estándar de los casos, con el de las siguientes intervenciones alternativas:

– suplementos diarios de hierro (H);
– quimioprofilaxis antipalúdica semanal con Deltaprim (combinación de 3,125 mg de pirimetamina y 25 mg de dapsona) (D); y
– una combinación de los dos tratamientos precitados (D + H).

El análisis económico se realizó utilizando como marco hipotético las intervenciones del Programa Ampliado de Inmunización (EPI). Las estimaciones incluyeron los costos de los servicios del dispensador de asistencia para cada intervención efectuada en la población atendida y los costos del tratamiento de los casos no prevenidos, junto con los gastos domésticos asociados al tratamiento de estos últimos casos. Para evaluar los costos de la actual estrategia de control basada en el manejo estándar de los casos se sumaron los costos del manejo de casos (relacionados con el dispensador de asistencia) y los gastos domésticos del tratamiento de los casos (costos directos e indirectos). En lo referente al dispensador de atención sanitaria, las relaciones costo-eficacia de la prevención de la anemia grave fueron las siguientes: US$ 7,9 por año de vida ajustado en función de la discapacidad (AVAD) con D + H; US$ 8,9 por AVAD con D; y US$ 21,0 por AVAD con H; en el análisis sociocultural (incluyendo también el gasto para las familias) las relaciones costo-eficacia se situaron entre los US$ 9 por AVAD de la opción D + H y los US$ 26 por AVAD de la opción H. En lo que respecta a la prevención de los episodios de paludismo sintomático durante el primer año de vida, las relaciones costo-eficacia fueron de US$ 9,7 y US$ 10,2 por AVAD con las estrategias D + H y D, respectivamente; en el análisis sociocultural se obtuvieron relaciones costo-eficacia de US$ 11 y US$ 12 por AVAD con las opciones D + H y D, respectivamente. Todas las intervenciones preventivas fueron más económicas que la estrategia de control basada únicamente en el manejo estándar de los casos, pero la combinación de hierro y quimioprofilaxis antipalúdica fue la más eficaz tanto en términos absolutos como en relación con el costo. Cuando el costo del manejo terapéutico era superior a US$ 8,5 para la anemia grave y a US$ 8 para los episodios de paludismo sintomático, la opción D + H resultaba más eficiente que el manejo estándar, cualquiera que fuese el nivel de eficacia de este último. La administración de antipalúdicos y de suplementos de hierro a los lactantes es una opción muy eficiente para los países con pautas de transmisión del paludismo y estructuras sanitarias similares a las del distrito de Kilombero. Este análisis económico respalda la inclusión tanto de la quimioprofilaxis como de los suplementos de hierro administrados a través del EPI en las estrategias de lucha contra el paludismo y la anemia.

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Annex
Cost analysis for standard case management of severe anaemia and clinical malaria episodes: costs for the health care provider

Case management for severe anaemia

- Consumable costs
  (a) For non-invasive treatment (i.e. iron, chloroquine, folic acid, laboratory material such as slides, lancets, material for determination of packed cell volume, blood smear, etc.) the costs amount to US$ 0.70 (1996 values). This figure should be used in the management of all cases, irrespective of transfusion requirements.
  (b) For transfusion (materials such as slides, blood lancet, butterfly clamp, human immunodeficiency virus (HIV) test for donor, blood donor set, blood receiving set, etc.) the costs amount to US$ 4.66.
- The criterion for transfusion is an erythrocyte volume fraction <15%. The proportion of severe anaemia episodes that will receive transfusion is 21.7%.

Thus the average consumable cost to the health care provider in respect of severe anaemia treatment is:

US$ (0.71 + (4.66 x 0.217)) = US$ 1.71 per episode of severe anaemia. This is a weighted average cost, taking into account cases that need transfusion and cases that do not.

Additional costs and assumptions are as follows.

- For hospitalized children, medical personnel are needed for 3 days and a laboratory technician is required for one day.
- Hospitalized children represent 30% of all severe anaemia cases; the length of stay is 3 days.
- Other hospital overheads (food, electricity, water, linen, maintenance, etc.) amount to US$ 1.47 per episode.
- All recurrent costs (doctor, nurse, laboratory technician and hospital overheads) amount to US$ 47.5 per episode for hospitalized children. Other recurrent costs for all patients amount to US$ 0.16.
- Capital costs (buildings, equipment) amount to US$ 0.57 per patient. These have been estimated on the basis of a 5-year amortization of buildings and basic equipment.

The total cost of severe anaemia case management is: US$ (1.71 + 0.3 x (0.57 + 47.5) + 0.16) = US$ 16.29 per severe anaemia episode in infants under 1 year of age.

Case management for clinical malaria episodes

- Approximately 60% of infants are hospitalized (unpublished data for Kilombero District), in accordance with WHO criteria for hospitalization.
- Hospitalized cases require treatment with intravenous quinine and sulfadoxine/ pyrimethamine (Fansidar).
- Depending on severity, patients have a mean hospital stay of 1–3 days.
- Severe malaria cases represent 9% of all episodes.
- Standard case management for non-severe, non-complicated malaria involves treatment with chloroquine, and consumable costs amount to US$ 0.43; 43% of cases are treated in this fashion.
- Non-severe but hospitalized cases are treated with chloroquine and quinine. Consumable costs amount to US$ 0.82; 49% of cases are treated in this way.
- Severe malaria is treated with quinine and Fansidar. The length of hospitalization is four to seven days. The consumable costs amount to US$1.38.

The weighted average for consumable costs is thus: US$ ((0.43 x 0.43) + (0.49 x 0.82) + (0.09 x 1.38)) = US$ 0.70.

- Other weighted recurrent costs amount to US$ 12.75.
- Capital costs per hospitalized patient amount to US$ 0.57.
- Hospital overheads per patient amount to US$ 1.47.

Total case management costs for a clinical malaria episode are:

US$(0.70 + 12.75 + 0.57 x (0.57 + 1.47)) = US$ 14.6 per clinical malaria episode in infants under 1 year of age.