The cost-effectiveness of antenatal malaria prevention in sub-Saharan Africa

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Two chemoprophylactic treatments for antenatal malaria prevention in sub-Saharan countries were examined. The two treatments, chloroquine (CQ) and sulfadoxine-pyrimethamine (SP), were administered as an addition to standard antenatal care (ANC). The regimens considered were a weekly CQ dose of 300 mg, with tablets prescribed at ANC visits and taken home by women, and two doses of SP (1,500 or 75 mg), taken during ANC visits.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of primigravidae attending ANC in sub-Saharan countries.

Setting
The setting was primary care. The economic study was carried out in the UK and applied to sub-Saharan countries.

Dates to which data relate
The clinical data were derived from studies published between 1982 and 1998. The majority of the cost and resource use data were derived from sources published between 1991 and 1997. The price year was 1995.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' assumptions.

Modelling
The authors stated that a standardised modelling framework was developed to provide estimates of the cost-effectiveness of the two prophylactic regimens in an operational setting with moderate to high malaria transmission.

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the mean birth weight and standard deviation (SD) in unprotected primigravidae,
- the increase in birth weight,
- the stillbirth rate in primigravidae,
the probability of an initial clinic visit in the first or second trimester,
the probability of returning for a second clinic visit,
the probability of returning for a third clinic visit,
the probability of compliance with CQ, and
life expectancy.

Study designs and other criteria for inclusion in the review
It would appear that the primary studies were identified selectively. It was not stated whether a systematic review of the literature was undertaken. Limited information on the design and characteristics of the primary studies was reported. Some evidence came from a published systematic review, while life expectancy came from life tables.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Ten primary studies provided clinical evidence.

Methods of combining primary studies
The primary studies appear to have been combined using a narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
The mean birth weight in unprotected primigravidae was 2.788 kg (SD 0.082; minimum 2.690, maximum 2.875). The mean SD of birth weight was 0.476 kg (SD 0.098; minimum 0.36, maximum 0.57).

The mean increase in birth weight was 0.101 kg (SD 0.042; minimum 0.003, maximum 0.198).

The stillbirth rate in primigravidae ranged from 0.062 to 0.116.

The best estimate for the probability of an initial clinic visit in the first or second trimester was 0.868 (minimum 0.540, maximum 0.936).

The best estimate for the probability of returning for a second clinic visit was 0.937 (minimum 0.835, maximum 0.989).

The best estimate for the probability of returning for a third clinic visit (relevant where human immunodeficiency virus
The prevalence was high) was 0.796 (minimum 0.481, maximum 0.942).

The probability of compliance with CQ ranged from 0.25 to 0.57.

The life expectancy at birth was 50 years for very-low-income and middle-income countries, and 65 years for higher income countries.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used to derive some clinical estimates used in the decision model.

**Estimates of effectiveness and key assumptions**
The probability of compliance with SP ranged from 0.85 to 0.95 per dose. It ranged from 0.72 to 0.90 for two doses of SP, and from 0.61 to 0.86 for three doses of SP. The proportion of underdosed cases that were effective ranged from 0.1 to 0.3.

Other assumptions were also made, but were mixed with published data and were used in specific equations to derive clinical estimates. Parasitological resistance (PR) was set between 0 (complete sensitivity) and 0.99 (complete resistance).

**Measure of benefits used in the economic analysis**
The summary benefit measure was the number of discounted years of life lost (DYLLs). These were estimated using the modelling framework. Some algorithms were used to transform birth-weight-specific neonatal mortality into DYLLs, taking the effects of the antimalarial drugs into consideration. An annual discount rate of 3% was applied.

**Direct costs**
The costs were annualised using an annual discount rate of 3%. The quantities of resources used were presented separately from the unit costs. The economic evaluation comprised all costs added to an existing ANC programme, and included the cost of staff training, the production of health education materials, drugs and incremental staff time. Drug-related side effects were not considered, because their impact was modest. A detailed breakdown of the cost items was provided. The cost/resource boundary of a third-party payer appears to have been adopted. The resource use and cost data came from reviews of published and unpublished literature, programme budgets, price catalogues, and consultation with researchers and programme managers. The costs were assumed to have been independent of compliance. All the costs were converted into 1995 values using the US Consumer Price Index. A budget impact analysis was implemented in a country such as Tanzania (population of 29.2 million; crude birth rate of 42.6 per 1,000; 17% of all births born to primigravidae; 93.2% of primigravidae and 91.8% of all pregnant women receive ANC; 70% of population at high risk of malaria; government health budget per annum of $94 million; no cost recovery).

**Statistical analysis of costs**
The costs were presented as mean values but were assigned a probabilistic distribution that was used in the sensitivity analysis.

**Indirect Costs**
The indirect costs were not considered in the economic evaluation.

**Currency**
The costs were converted into US dollars ($) using the exchange rate for 1995.
Sensitivity analysis
A probabilistic sensitivity analysis was carried out using a Monte Carlo simulation, assigning a probabilistic distribution to all model inputs. This resulted in mean cost-effectiveness ratios and 90% ranges of values. Two alternative intervention scenarios were considered, a 2-dose regimen for all pregnant women and a 3-dose regimen for all pregnant women. The ranges of values used were derived from the literature.

Estimated benefits used in the economic analysis
At complete drug sensitivity (PR=0), the DYLLs averted per primigravida with the CQ regimen were on average 0.09 for very-low- and middle-income countries, and 0.10 for higher income countries.

With the 2-dose SP regimen for primigravidae, 0.14 DYLLs were averted per primigravida for very-low- and middle-income countries, and 0.16 for higher income countries. SP was more effective than CQ even when there was no resistance to either drug. The DYLLs were higher for higher income than low- and middle-income countries, owing to a higher life expectancy.

Cost results
At complete drug sensitivity (PR=0), the expected incremental cost per primigravidae with CQ was $1.30 for very-low-income countries, $1.42 for middle-income countries and $2.31 for higher income countries.

The expected incremental cost per primigravidae with SP (with PR=0) was $1.13 for very-low-income countries, $1.25 for middle-income countries and $2.14 for higher income countries. Thus, SP was cheaper for all countries, regardless of the level of income. The analysis showed that drugs were the main cost drivers in very-low- and middle-income countries, while salaries remained the most important cost category in higher income countries.

The budget impact analysis showed that the weekly dose of CQ would cost $179,349 per annum (0.19% of government health budget), while the 2-dose regimen of SP would cost $155,896 (0.17% of government health budget). The corresponding figure for a 2-dose regimen for all pregnant women was $913,535 (0.97% of government health budget), and for a 3-dose regimen for all pregnant women, $1,119,080 (1.19% of government health budget).

Synthesis of costs and benefits
The costs and benefits were combined by calculating the incremental cost per primigravida divided by the number of DYLLs averted with each drug over no intervention.

At complete drug sensitivity (PR=0), the cost per DYLL averted with CQ was $21 (range: 7 - 49) in very-low-income countries, $23 (range: 8 - 52) in middle-income countries and $34 (range: 12 - 75) in higher income countries.

The cost per DYLL averted with SP was $12 (range: 4 - 27) in very-low-income countries, $13 (range: 4 - 29) in middle-income countries and $20 (range: 7 - 43) in higher income countries.

The authors stated that CQ was slightly less effective than SP because of fewer DYLLs averted and higher costs. Considering a threshold of $150 per DYLL as efficient for all income levels, with no resistance, either regimen would be considered an "attractive" option for all economic strata.

When allowing for drug resistance, effectiveness was reduced and the cost-effectiveness ratios increased. The cost-effectiveness range for the CQ regimen remained lower than $150 for up to 67% resistance, and the SP regimen up to 82%. With a 2-dose regimen, the cost-effectiveness range at zero resistance was $12 to $70, and the level of resistance up to which the cost-effectiveness range remained lower than $150 fell to 54%. With a 3-dose regimen given to all gravidae, the cost-effectiveness range at zero resistance increased to $22 to $129, reducing the $150 threshold to 14% resistance.

Authors' conclusions
The use of the sulfadoxine-pyrimethamine (SP) regimen as antenatal malaria prevention for primigravidae appears to
have been more cost-effective than the chloroquine (CQ) regimen, owing to lower costs and higher compliance. However, both prophylactic treatments represented good value for money in the context of developing countries.

CRD COMMENTARY - Selection of comparators
The authors justified the selection of the comparators. CQ was the typical prophylactic treatment for antenatal malaria prevention, while SP represented an alternative preventive strategy. Both options were compared with no intervention, but were not directly compared with each other. The dosages were clearly reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came mainly from published evidence. However, it was not stated whether a systematic review of the literature had been undertaken to identify the primary studies. One of the sources used was a published review, but information on the other studies was not provided. The primary studies appear to have been combined using some algorithms, but differences across the studies were not highlighted. Few estimates were based on authors’ assumptions. All of the clinical inputs were varied in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure was appropriate for assessing the impact of the interventions on patient survival, and is comparable with the benefits of other health care interventions. Discounting was applied. Quality or disability adjustments were not considered. The authors noted that some benefits of the interventions (i.e. increased survival for children older than 28 days and potential benefits from reductions in morbidity and mortality for mothers) were not considered in the analysis.

Validity of estimate of costs
The perspective adopted in the study appears to have been that of the third-party payer as all the costs included in the analysis were relevant to the public sector. Extensive details of the cost analysis, such as the unit costs, quantities of resources used, price year and source of data, were reported. This enhances the possibility of replicating the analysis and refitting the main results. The cost estimates were specific to the study setting but ranges of values were considered in the probabilistic sensitivity analysis.

Other issues
The authors made some comparisons of their findings with those from studies that evaluated other malaria preventive interventions. The issue of the generalisability of the study results was addressed, not only in the sensitivity analysis but also by considering different economic strata and alternative resistance levels. The authors noted some limitations of their study. First, the impact on child survival was not empirically demonstrated. Second, the impact of human immunodeficiency virus was not explicitly modelled. It was assumed in the cost analysis that ANC services were already in place.

Implications of the study
The study results supported the use of SP or CQ for antenatal malaria prevention in sub-Saharan Africa. The authors stressed that further research should investigate potential tools to improve compliance with treatment, as well as potential replacement drugs to enable the provision of effective antenatal malaria prevention in the future.

Source of funding
Supported in part by the Global Forum for Health Research, with a grant provided by the World Bank.

Bibliographic details

**PubMedID**
11425177

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Africa South of the Sahara; Antimalarials /administration & dosage /economics; Chloroquine /administration & dosage; Cost-Benefit Analysis; Drug Combinations; Female; Health Services Accessibility /economics; Humans; Infant, Newborn; Malaria /economics /prevention & control; Models, Economic; Pregnancy; Pregnancy Complications, Parasitic /economics /prevention & control; Preventive Health Services /economics; Pyrimethamine /administration & dosage; Sulfadoxine /administration & dosage

**AccessionNumber**
22001001314

**Date bibliographic record published**
31/10/2005

**Date abstract record published**
31/10/2005