Cost-effectiveness of sulfadoxine-pyrimethamine for the prevention of malaria-associated low birth weight


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
Several strategies for the prevention of low birth weight (LBW) due to placental malaria in pregnant primigravidae and secundigravidae, were examined. The strategies were:

- two-dose sulfadoxine-pyrimethamine (SP), with one dose given at the first antenatal clinic (ANC) visit, usually occurring in the second trimester, and a second dose given early in the third trimester;
- monthly SP, with the first dose given at the first ANC visit, followed by monthly dosing through the ninth month of gestation;
- human immunodeficiency virus (HIV) testing followed by SP treatment according to HIV serostatus (two doses for HIV-negative women and monthly doses for HIV-positive women); and
- febrile case management (CM), in which women were treated for malaria when they have fever accompanied by parasitaemia during pregnancy.

Each SP treatment dose consisted of an oral dose of 1,500 mg sulfadoxine and 75 mg pyrimethamine.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study sample comprised a hypothetical cohort of pregnant women attending an ANC whose individual HIV serostatus was unknown.

Setting
The setting was primary care. The economic study was carried out in the USA and Kenya.

Dates to which data relate
The effectiveness data were derived from studies published between 1983 and 2000. Some resource use and cost data were obtained from sources published between 1980 and 1999. The price year was 1997.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies and authors' assumptions.
Modelling
A decision analysis tree was constructed to examine the cost-effectiveness of the five alternative strategies under evaluation in a hypothetical cohort of 10,000 pregnant women. The model was populated with data derived mainly from the literature. The model considered the probabilities of developing placental parasitaemia in HIV-positive or HIV-negative women. The final end point was the potential development of an LBW infant. The structure of the model was reported.

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

maternal HIV prevalence,
the probability of ANC visits,
the positive and negative predictive value of the enzyme-linked immunosorbent assay (ELISA) procedure,
the proportion of women consenting to HIV testing,
the rate of placental parasitaemia,
the incidence of LBW,
normal birth weight mortality and LBW mortality, and
the disability-adjusted life expectancy (DALE).

Study designs and other criteria for inclusion in the review
The authors stated that a review of the existing literature and unpublished studies was undertaken to derive primary estimates. It was unclear whether the review was systematic. Information on the design and characteristics of the primary studies was not reported.

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
Eighteen primary studies provided the clinical inputs.

Methods of combining primary studies
A narrative method appears to have been used to combine the primary studies.

Investigation of differences between primary studies
Not stated.
Results of the review

The maternal HIV prevalence rate was 0.270 (range: 0.010 - 0.340).

The probability of one ANC visit was 0.950 (range: 0.300 - 0.950) and the probability of two ANC visits was 0.900 (range: 0.200 - 0.900). The probability of 3 or more ANC visits was 0.100 (range: 0.100 - 0.875).

The positive predictive value of the ELISA procedure was 0.998 and the negative predictive value was 0.999.

The proportion of women consenting to HIV testing was 0.800 (range: 0.60 - 1.00).

The rate of placental parasitaemia in HIV-positive women was 0.490 (range: 0.399 - 0.581) without a dose, 0.357 (range: 0.266 - 0.448) with one dose, 0.188 (range: 0.118 - 0.258) with 2 doses, and 0.051 (range: 0.026 - 0.076) with 3 or more doses.

The rate of placental parasitaemia in HIV-negative women was 0.232 (range: 0.189 - 0.275) without a dose, 0.112 (range: 0.072 - 0.152) with one dose, 0.078 (range: 0.047 - 0.109) with 2 doses, and 0.051 (range: 0.026 - 0.076) with 3 or more doses.

The incidence of LBW was 0.300 (range: 0.130 - 0.390) with and 0.180 (range: 0.080 - 0.200) without placental parasitaemia.

The normal birth weight mortality was 0.023 (range: 0.007 - 0.023) in the neonatal period and 0.103 (range: 0.009 - 0.103) in the postneonatal period. The LBW mortality was 0.051 (range: 0.041 - 0.051) in the neonatal period and 0.138 (range: 0.031 - 0.138) in the postneonatal period.

The estimated DALE was 39.4 years (range: 29 - 49). The DALE was discounted at a rate of 3%.

Methods used to derive estimates of effectiveness

The authors made some assumptions to derive model inputs.

Estimates of effectiveness and key assumptions

The rate of LBW infants hospitalised was 1 (range: 0 - 1). It was assumed that infants who did not survive the postneonatal period lost their full DALE. Thus, each LBW-associated death resulted in a loss of 23.62 discounted disability-adjusted life-years (DALYs).

Measure of benefits used in the economic analysis

The summary benefit measures used were the expected number of LBW infants prevented by each strategy and the DALYs saved by each strategy. Both measures were obtained using a modelling approach.

Direct costs

Discounting does not appear to have been relevant since the costs were incurred during a timeframe shorter than two years. The unit costs were not presented separately from the quantities of resources used for all items. The health services in the economic evaluation included HIV testing and counselling, SP therapy and excess health care for a LBW infant. HIV testing and counselling including two ELISAs, pre- and post-test counselling. SP therapy included the drug cost and the costs of shipping, handling and insurance. Excess health care for a LBW infant included only the hospitalisation costs and excluded all costs incurred after hospital discharge. The cost of an ANC visit was not included because SP would be administered during routine ANC visits.

The cost/resource boundary of the health care system was adopted. Resource use was derived from authors' assumptions based on both published and unpublished studies. In particular, it was assumed that where no ANC malaria care was available, no health care for LBW infants was available. The costs came from published sources, including publications.
by the World Health Organization. The price year was 1997 and all costs from previous years were adjusted using a 5% annual inflation rate.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate sensitivity analyses were carried out on all model inputs to examine the robustness of the cost-effectiveness ratios to variations in the base-case assumptions. Multivariate sensitivity analyses were also performed to represent the range of conditions found in sub-Saharan Africa. Estimates changed in multivariate analyses were:

- the HIV seroprevalence in pregnant women,
- the percentage of pregnant women attending an ANC and receiving malaria treatment,
- the incidence of LBW,
- the rates of placental parasitaemia,
- the cost of HIV testing and counselling,
- the cost of SP,
- the probability that a LBW infant would be hospitalised following delivery,
- the costs of treating LBW infants, and
- country-specific DALEs.

The ranges of values used in the analysis were derived from the literature, or based on authors’ assumptions.

**Estimated benefits used in the economic analysis**
In a cohort of 10,000 pregnant women, the number of LBW cases was 2,162 with no ANC care for malaria, 2,135 with CM, 1,963 with two-dose SP, 1,915 with HIV testing and SP treatment, and 1,906 with monthly dose SP.

In a cohort of 10,000 pregnant women, the number of DALYs lost was 32,381 with no ANC care for malaria, 32,241 with CM, 32,141 with two-dose SP, 32,104 with HIV testing and SP treatment, and 32,070 with monthly dose SP.

**Cost results**
In a cohort of 10,000 pregnant women, the total costs were $0 with no ANC care for malaria, $95,400 with CM, $93,300 with two-dose SP, $150,640 with HIV testing and SP treatment, and $92,600 with monthly dose SP.

In a cohort of 10,000 pregnant women, the total programme costs (including costs of ANC malaria care only) were $0 with no ANC care for malaria, $1,400 with CM, $2,700 with two-dose SP, $7,000 with HIV testing and SP treatment,
Synthesis of costs and benefits

Incremental cost-effectiveness ratios and cost-utility ratios were calculated to combine the costs and benefits of the alternative strategies. Each strategy was compared with the next less effective option. Average cost-utility ratios were also reported.

The incremental cost per LBV case prevented with CM over no ANC care for malaria was $3,533. Two-dose SP was dominant over CM. HIV testing and SP treatment was dominated by two-dose SP, while monthly dose SP was dominant over two-dose SP.

The incremental cost per DALY gained (when only the programme costs were considered) was $10 with CM over no ANC care for malaria and $13 with two-dose SP over CM. HIV testing and SP treatment was dominated by two-dose SP. The incremental cost per DALY gained was $23 with monthly dose SP over two-dose SP.

The average cost per DALY gained was $10 with CM, $11 with two-dose SP, $25 with HIV testing and SP treatment, and $14 with monthly dose SP.

The ranking of the alternative strategies did not change in the sensitivity analysis, and the monthly SP strategy remained the most cost-effective. The analysis revealed that the probabilities that placental parasitaemia would result in LBW and that pregnant women would have access to and accept SP were the factors with the greatest impact on the effectiveness results. On the other hand, the costs were mostly affected by the probability that a LBW infant would be hospitalised after delivery, the costs associated with a LBW infant, the cost of SP, and the probability that placental parasitaemia would result in LBW.

Monthly SP remained cost-effective regardless of HIV seroprevalence, and the cost per DALY gained remained below the value of $25, a range still considered cost-effective. The cost-effectiveness of all strategies could be improved by efforts to increase access to and acceptance of any of the preventive options.

Authors' conclusions

The use of monthly sulfadoxine-pyrimethamine (SP) to prevent malaria-associated morbidity and mortality was a cost-effective strategy in high malaria transmission areas. The cost-effectiveness of monthly SP compared favourably with that of other malaria interventions.

CRD COMMENTARY - Selection of comparators

The authors justified the choice of the comparators examined in the study and discussed the reasons for different SP regimens considered in the analysis. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The analysis of effectiveness was based on data derived from several sources, including published and unpublished studies. It was not explicitly stated whether the review of the literature was systematic. However, no details on the design and characteristics of the studies were provided. This limits the possibility of assessing the validity of the sources used. Similarly, the methods used to extract and combine the primary estimates were not described. Some key assumptions were also made. The impact of changing the base-case assumptions was appropriately investigated in the sensitivity analysis.

Validity of estimate of measure of benefit

Two summary benefit measures were used, LBW cases and DALYs. While the former (LBW cases) is a disease-specific measure, the latter (DALYs) is more generalisable and comparable with the benefits of other health care interventions in developing countries.
Validity of estimate of costs
The authors stated explicitly which perspective was adopted in the study. As such, all the relevant categories of costs were considered. The unit costs were presented separately from the quantities of resources used for most items. The price year was reported, which enhances the possibility of replicating the study analysis and results in other settings. The costs were treated deterministically, but sensitivity analyses were carried out on the cost estimates. The source of the data was provided. It was noted that some cost estimates could have been overestimated. However, the conclusions of the analysis were robust to changes in the economic inputs. Further, the exclusion of training costs for health care workers and the costs for health education of the community biased the results against the SP regimen, since such costs would have been higher for the HIV testing approach. The authors justified the exclusion of the costs of adverse drug reactions.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was addressed in the sensitivity analysis. The authors noted some limitations to the validity of their analysis. For example, the lack of an evidence-based significant decrease in the incidence of LBW with intermittent presumptive treatment using SP. However, it was stated that a clear trend towards such a reduction had been observed. The study results referred to primigravidae and secundigravidae, and this was reflected in the authors’ conclusions.

Implications of the study
The study results supported a preventive strategy of administering two-dose or monthly dose presumptive SP treatment to primigravidae and secundigravidae in the second and third trimesters of gestation in order to reduce the incidence of malaria-associated LBW. Cost-savings could be realised even in areas of low malaria transmission.

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Other publications of related interest

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MeSH
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