Cost-effectiveness of the introduction of a pre-erythrocytic malaria vaccine into the expanded program on immunization in sub-Saharan Africa: analysis of uncertainties using a stochastic individual-based simulation model of Plasmodium falciparum malaria

Maire N, Shilcutt SD, Walker DG, Tediosi F, Smith TA

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.

CRD summary
The study objective was to assess the cost-effectiveness of introducing the Pre-Erythrocytic Malaria Vaccine into the Expanded Programme of Immunisation in Sub-Saharan Africa. The authors concluded that the vaccine's cost-effectiveness will be maximal in low endemicity. Overall the quality of the study methodology was good and they and the results were appropriately reported. Given the scope of the study, the authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to assess the cost-effectiveness of introducing the Pre-Erythrocytic Malaria Vaccine (RTS, S) into the Expanded Programme of Immunisation in Sub-Saharan Africa.

Interventions
The authors compared two interventions: a pre-erythrocytic vaccine (RTS, S) that modifies the risk that a human host becomes infected when bitten by an infectious mosquito; and current practice (no vaccination). Simulated delivery of the vaccine was at ages one, two and three months (three doses).

Location/setting
Sub-Saharan Africa/Community care.

Methods
Analytical approach:
The authors reported that a previously published stochastic simulation model was used to model the natural history and epidemiology of Plasmodium falciparum (Maire et al. 2006a, see Other Publications of Related Interest). The time horizon of the study was 10 years. A societal perspective was adopted. Vaccination was simulated in populations of 100,000 people at 10 different entomological inoculation rates (EIRs) to measure exposure to the infective stage of the parasite (number of infectious bites per annum).

Effectiveness data:
Clinical and effectiveness data were derived from previously published studies. Most of the model parameter data was that used in the original published model evaluating the natural history and epidemiology of P falciparum (Maire et al. 2006a). The main measure of effectiveness used in the study was the vaccine efficacy after one, two and three doses. This estimate was derived from a previously published study based on initial field data (Maire et al. 2006b, see Other Publications of Related Interest).

Monetary benefit and utility valuations:
The authors reported that the health outcomes simulated (uncomplicated episodes, severe episodes and deaths) were translated to disability-adjusted life years (DALYs). The disability weights were the same as those as used in a previously published analysis by the authors (Tediosi et al. 2006, see Other Publications of Related Interest).

Measure of benefit:
Disability Adjusted Life Years (DALYs) averted. Future benefits were discounted using an annual rate of 3%.

Cost data:
The authors reported that provider and out-of-pocket patient costs were included in the analysis. The authors considered the costs of medications (ACT and quinine dihydrochloride), outpatient visits (health centres, hospitals and dispensaries), hospitalisation, vaccine, vaccine storage, distribution and delivery and training. Resource use such as in-patient rates, length of stay and outpatient care rates were derived from published studies and reports. Cost information was derived from previous work undertaken by the authors, published reports and studies. The price year was 2008. All costs were reported in international dollars ($). Future costs were discounted using an annual rate of 3%.

Analysis of uncertainty:
The authors undertook a probabilistic sensitivity analysis by fitting probability distributions alongside all model parameters. One thousand simulations were performed. The results were presented using cost-effectiveness acceptability curves. The authors performed an Expected Value of Perfect Information (EVPI) analysis to quantify the value of acquiring additional information on the parameters.

Results
When compared to no vaccination, the total discounted DALYs averted with vaccination ranged from 754.1 at an entomological inoculation rate (EIR) of 0.131 to 14,602.9 at an EIR of 5.25. Above an EIR of 5.25, the number of DALYs averted diminished to 1,201.2 at an EIR of 168. At and above EIRs of 252 more DALYs were gained than averted using vaccination.

When compared to no vaccination, the additional discounted costs of vaccination ranged from $960,300 at an EIR of 0.131 to $991,200 at an EIR of 420.

Costs and benefits were combined using an incremental cost-utility ratio (additional cost per DALY averted). When compared to no vaccination, the additional cost per DALY averted with vaccination ranged from $1,065.8 at an EIR of 0.131 to $52.3 at an EIR of 5.25. At or above EIRs of 252, vaccination was dominated by no vaccination (was more costly and less effective).

Results of the probabilistic sensitivity analysis showed that at a threshold of $207 per DALY averted the probability of vaccination being cost-effective ranged from 52.4% to 65.9% depending on the distribution of EIR.

The authors reported that the EVPI was substantial and that accrual of information on local endemicity to guide deployment decisions would be highly efficient.

Authors' conclusions
The authors concluded that the cost-effectiveness of RTS, S would be maximal in low endemicity settings (EIR of two to 20 infectious bites per annum).

CRD commentary
Interventions:
The interventions under study were reported adequately. The comparators were selected appropriately: the usual state in the authors’ setting (no vaccination) was compared with the proposed vaccination strategy.

Effectiveness/benefits:
The authors reported that a previously published stochastic simulation model was used to model the natural history and epidemiology of *P. falciparum*. The authors used many of the parameter values from the original model. The authors adequately reported for each model parameter its base case value, the distribution used for the probabilistic sensitivity analysis and the source from which it was derived. The main measure of effectiveness was adequately reported. The authors did not report whether the sources of information in the previous model and those used to supplement it for the current study were identified through a systematic review of the literature. As a result, it is not possible to determine whether all relevant information was included in the study. DALYs are generally considered to be a valid benefit measure (especially for developing countries). They capture the burden of disease and allow cross-disease comparisons to be made. The authors provided references for the sources of disability weights but did not describe how these were
assessed, which would have been informative. It was unclear whether a time horizon of 10 years was sufficient to capture all the differences in costs and effectiveness.

Costs:
The perspective adopted in the economic analysis was explicitly reported to be that of society. The authors included only direct medical costs paid either by healthcare providers or out-of-pocket by patients or their relatives. Indirect costs such as informal care giving and productivity losses due to early mortality or absence from work were not included in the analysis. The sources from which costs and resource use were derived were reported adequately. The price year, time horizon, discount rate used and currency details were all reported explicitly.

Analysis and results:
The authors reported that cost and outcome information were synthesised by use of a previously published model. Adequate details of the model were provided and included references. No graphical depiction was provided. The authors appropriately assessed model uncertainty and the value of conducting further research using probabilistic sensitivity and EVPI analyses. As a main limitation to their study the authors reported that the parameters of the model were sampled independently of each other despite correlations in the fitted values.

Concluding remarks:
The quality of the study methodology was good and these and the results were appropriately reported. Given the scope of the study, the authors' conclusions appear to be appropriate.

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