The cost-effectiveness of screening blood donors for malaria by PCR
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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
The use of polymerase chain reaction (PCR) for screening blood donors for malaria.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised potential blood donors. No further characteristics of the study population were described.

Setting
The setting of the study was not unclear, but PCR techniques are probably performed in a secondary care setting.

Dates to which data relate
The effectiveness data were derived from literature published from 1998 to 2001. The resource use data were mainly derived from studies published from 1995 to 1998. Prices relating to 2000-2001 were used.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies. Many estimates of effectiveness were based on opinion.

Modelling
A decision analysis model was developed to compare the costs and effectiveness of the four screening strategies examined. The model was structured as a decision tree. The number of cases of malaria transmission averted due to screening, and the number of deferred donors due to positive results of screening tests, were estimated for each strategy assessed.

Outcomes assessed in the review
The outcomes assessed were:

the prevalence of malaria infection among blood donors,

the transmissibility of malaria, and
the test characteristics (sensitivity and specificity) of the standard questionnaire, and of PCR used for screening blood donors for malaria.

Study designs and other criteria for inclusion in the review
Not stated.

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
Approximately three primary studies were included in the review.

Methods of combining primary studies
The data were taken selectively from the literature.

Investigation of differences between primary studies
There was no reference to any differences between the primary studies included in the review.

Results of the review
The prevalence of malaria infection among blood donors was 3.8 x10^-5 (range: 1.0 x10^-5 - 7.0 x10^-5).

The transmissibility of malaria was 100% (range: 10 - 100%).

The sensitivity of the screening questionnaire in identifying malaria cases was 0.8 (range: 0.1 - 1.0) and the specificity was 0.997 (range: 0.9 - 1.0).

The sensitivity of PCR was 0.90 (range: 0.5 - 1.0) and the specificity was 0.997 (range: 0.9 - 1.0).

The range of values reflected the uncertainty associated with the point estimates of each variable due to the lack of published data. Consequently, most point estimates were based on assumptions.

Methods used to derive estimates of effectiveness
The authors made assumptions to derive some estimates of effectiveness.

Estimates of effectiveness and key assumptions
The prevalence of malaria infection among blood donors had not been determined in the literature and was therefore estimated from the incidence of malaria in the Canadian population. The sensitivity and specificity of the standard screening questionnaire had also not been established and were determined from data on transfusion-transmitted malaria. The sensitivity of PCR as a screening method for malaria and the transmission rate of malaria were based on
assumptions, as they had not been described in the published literature.

**Measure of benefits used in the economic analysis**
The benefit measure used was the number of cases of malaria transmission averted. This was also expressed as the probability of malaria transmission per blood donation.

**Direct costs**
The direct costs only included the costs to the health service. These covered the cost of malaria transmission, the cost of a potentially wasted blood donor (i.e. a donor that was deferred although he did not have malaria), the costs associated with the time spent in retrieving a unit of blood, and also with collecting a unit of blood that was discarded due to a false-positive test result, and the cost of PCR testing. The cost of the questionnaire was assumed to be zero since questions about travel and country of origin were a minor part of the questionnaire used to screen blood donors. The direct costs of malaria transmission were for physician visits, laboratory testing, hospitalisation, medications, emergency room visits and the recall of blood. The cost of adverse effects due to malaria medications was not considered. The cost of a potentially wasted blood donor reflected the need to recruit new blood donors during periods of blood shortages, and also potential increases in mortality and morbidity in patients requiring transfusion due to these shortages. The cost of retrieving a unit of blood accounted for the localisation and retrieval of blood products of donors who, after they had donated, contacted the blood centres with information of recent travel to a malaria endemic area. This included the total cost of the collection, production, distribution, delivery and disposal of units of blood.

The unit costs and the quantities were analysed separately in the case of malaria transmission costs. Resources used for malaria transmission were based on a study published in 1998 and further assumptions. The unit costs were derived from hospital data, governmental reports, Canadian guides on pharmaceutical prices, and other published sources. The cost of a potentially wasted blood donor was based on assumption. The cost of retrieval was derived from the Canadian Blood Service, 2001. The cost of collection was derived from literature published in 1996. The cost of PCR testing was based on expert opinion. The total cost associated with each strategy evaluated was derived using modelling. Discounting was not carried out, which was appropriate since the costs were incurred during less than one year. Prices relating to 2000-2001 were used.

**Statistical analysis of costs**
The costs were treated deterministically. No statistical analysis of the costs was performed.

**Indirect Costs**
The indirect costs expressed time lost from work for blood recipients due to malaria transmission. The average number of days lost from work was estimated, based on the expected clinical course of the disease. The unit cost attached represented the average daily wage, based on Statistics Canada - CANSIM. The quantities and the costs were reported separately. Discounting was not carried out as it was not necessary. The prices referred to the 2000-2001 currency year.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
A sensitivity analysis was carried out to examine the robustness of the results under the uncertainty associated with values based on assumptions. All input parameters (relating to both effectiveness and cost variables) were given a wide, conceivable range of values and were investigated in a one-way sensitivity analysis. In addition, a two-way sensitivity analysis was conducted by simultaneously varying the cost of a lost blood donor and the specificity of the PCR testing, to explore whether these changes had an impact on the results.
Estimated benefits used in the economic analysis
The number of transmitted malaria cases in 250,000 potential donors was 10 for no screening, 3 for the screening questionnaire, 3 to 4 for the screening questionnaire followed by PCR, and 2 for PCR screening.

The probability of malaria transmission per blood donation was $3.8 \times 10^{-5}$ for no screening, $0.8 \times 10^{-5}$ for the screening questionnaire, $0.8 \times 10^{-5}$ for the screening questionnaire followed by PCR, and $0.04 \times 10^{-5}$ for PCR screening.

Cost results
The cost per donor was $0.04 for no screening, $0.82 for the screening questionnaire, $0.24 for the screening questionnaire followed by PCR, and $15.92 for PCR screening.

These costs also included the costs associated with the loss of blood donors who were deferred, although they did not have malaria, due to false-positive screening tests.

Synthesis of costs and benefits
The estimated costs and benefits were combined in the form of incremental cost-effectiveness ratios (ICERs). The ICERs represented the incremental costs per case of malaria transmission averted.

The screening questionnaire was equally effective as the screening questionnaire followed by PCR, but was more costly. The screening questionnaire was therefore dominated and was not compared further with other strategies.

The ICER of the screening questionnaire followed by PCR compared with no screening was $6,463 per case of malaria transmission averted.

The ICER of PCR screening of all blood donors compared with the screening questionnaire followed by PCR was $3,972,624 per case of malaria transmission averted.

The results of the analysis were sensitive to the specificity of the screening questionnaire. When the sensitivity was 100%, the screening questionnaire became less costly than the screening questionnaire followed by PCR. The results were also sensitive to the cost of a lost donor. Changing the values of other variables in one-way sensitivity analyses affected the ICERs, but did not change the relative order of strategies in terms of their relative costs and effectiveness.

PCR screening remained the most costly option, with ICERs always above $200,000 when compared with the screening questionnaire followed by PCR. The two-way sensitivity analysis showed that, as the cost of a blood donor and the specificity of PCR both increased, the screening questionnaire followed by PCR became the least costly option. When the cost of a lost blood donor was under $27 and the specificity of PCR was at its lowest value (90%), then the standard screening questionnaire became less costly than the screening questionnaire followed by PCR. If the cost of a lost blood donor was valued above $27, then the screening questionnaire followed by PCR was the least costly strategy at the lowest specificity for PCR.

Authors' conclusions
The addition of polymerase chain reaction (PCR) to the standard screening questionnaire was economically attractive compared with the standard screening questionnaire.

CRD COMMENTARY - Selection of comparators
PCR screening was compared with three alternative strategies. One was no screening, which allowed for the active value of the assessed technology to be evaluated. The other two were a screening questionnaire, and the screening questionnaire followed by PCR in cases with high risk for malaria. The screening questionnaire represented the only available method for identifying blood donors at high risk for malaria in Canada. You should consider whether this strategy reflects widely used practice in your own setting.
Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. The number of primary studies used was very limited. Most of the input parameters used in the model were based on authors' assumptions, the authors justifying these assumptions with reference to relevant literature. All the estimates of effectiveness were investigated in sensitivity analyses. The ranges of values used appear to have been appropriate, and reflected the uncertainty associated with each input variable in the model.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The decision tree used for the analysis was appropriate for the study question, as it included all potential pathways for malaria transmission following a screening strategy, as well as pathways of events related to screening incurring additional costs (e.g. potentially wasted donors, or the retrieval and collection of blood after positive test results).

Validity of estimate of costs
It was stated that a societal perspective was adopted in the study. However, categories of cost such as direct non-health care costs for both blood donors and patients with malaria, and also potential time losses for blood donors, were not included in the analysis. The cost of adverse events due to malaria medication was not considered, although this probably did not affect the authors' conclusions since its contribution to the total costs was likely to be very low. The costs and the quantities were reported separately for malaria transmission, hence improving the generalisability of the results. Many cost elements were based on assumptions. A sensitivity analysis of the costs was conducted, using a wide range of values. Discounting was not carried out, which was appropriate since the costs were incurred during less than one year. The date to which the prices referred was reported. This enhances the reproducibility of the results.

Other issues
The authors did not compare their findings with those of other studies. The issue of generalisability of the results to other settings with a higher prevalence of transfusion-transmitted malaria was addressed. The authors reported a number of limitations of their study, mainly related to the key assumptions they made. However, the authors considered them to be a minor issue since the sensitivity analysis confirmed the robustness of the results. The authors reported that they did not consider the use of the immunofluorescent antibody test or the malaria antibody enzyme-linked immunosorbent assay as alternative strategies, although they were used in other countries. The authors appear to have presented their results adequately and their conclusions reflected the scope of the analysis.

Implications of the study
The authors recommended that screening blood donors with the standard questionnaire followed by PCR for high-risk cases should be considered an alternative strategy to the routine practice of the standard screening questionnaire alone. In addition, they suggested that large studies confirming the high sensitivity and specificity of PCR to blood donor populations are needed.

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