Cost-effectiveness of interventions to reduce vertical HIV transmission from pregnant women who have not received prenatal care

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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
A programme of rapid human immunodeficiency virus (HIV) testing (rapid HIV-1 antibody test), with administration of antiretroviral prophylaxis for those testing positive, was examined. The programme was offered to pregnant women presenting in labour without prenatal care, to prevent the potential vertical transmission of HIV to their infants. Antiretroviral prophylaxis consisted of zidovudine therapy. However, alternatives to the rapid test (i.e. empiric nevirapine treatment) and zidovudine therapy (nevirapine and combination therapy) were also considered.

Type of intervention
Diagnosis and primary or secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of pregnant women presenting in labour without prenatal care.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1991 and 2001. Some resource use data and costs were derived from studies published between 1994 and 2001. The price year was 2000.

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

Modelling
A decision tree model was constructed to identify all relevant clinical and economic outcomes associated with the two interventions under examination, in a cohort of 50,000 pregnant women presenting in labour without prenatal care. The average age of the cohort was 36 years. If infected, the CD4 cell count was 200 cells/microL. The impact of the interventions on both the mothers and their infants was assessed. The model structure included the possibility that women could accept or refuse tests. In addition, those who accepted could test positive (and then receive treatment) or test negative. Treatment could be adequate, or women could deliver before prophylaxis was effective. Finally, in truly HIV-infected mothers, there was a chance of HIV transmission to infants. The model of delivery (either vaginal or nonselective Caesarean section) had no impact on the model outcomes. The structure of the tree was reported.
Outcomes assessed in the review
The outcomes assessed from the literature were:

the prevalence of HIV in women without prenatal care;

HIV transmission without intervention;

the relative risk reduction in transmission with prophylactic therapy;

the sensitivity and specificity of the rapid HIV test;

the willingness to accept rapid HIV testing;

the proportion of women delivering before treatment was effective; and

the discounted (3%) quality-adjusted life-years (QALYs) for HIV-infected infants, uninfected infants, HIV-infected women, and uninfected women.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature had been undertaken to identify relevant studies. No specific inclusion criteria were presented. Details of the designs of the primary studies were not provided. Life expectancy was derived 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
Nineteen primary studies provided evidence.

Methods of combining primary studies
A narrative method was used to combine the primary estimates.

Investigation of differences between primary studies
Not stated.

Results of the review
The prevalence of HIV in women without prenatal care was 5.1/1,000 (range: 0.1 - 50/1,000). The rate of HIV transmission without intervention was 26.6% (range: 15 - 30).

The relative risk reduction in transmission with prophylactic therapy was 0.62 (range: 0 - 1).

The sensitivity of the rapid HIV test was 0.999 (range: 0.99 - 0.999) and the specificity was 0.996 (range: 0.89 - 0.999).
The willingness to accept rapid HIV testing was 0.86 (range: 0 - 1).

The proportion of women delivering before treatment was effective was 0.25 (range: 0 - 1).

The estimated QALYs were 9.7 (range: 6.8 - 24.8) for HIV-infected infants, 29.7 (range: 15 - 30) for uninfected infants, 7.6 (range: 6 - 20) for HIV-infected women, and 22.6 (range: 10 - 25) for uninfected women.

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

Estimates of effectiveness and key assumptions
The authors assumed:

- nevirapine would have the same efficacy as zidovudine in reducing HIV transmission;
- the same proportion of women would deliver before the drug took effect;
- minimal counselling would be required; and
- all infants would require full testing (2 serial HIV polymerase chain reaction tests) to exclude HIV infection.

Measure of benefits used in the economic analysis
The summary benefit measure was the number of QALYs associated with the intervention versus no intervention. An annual discount rate of 3% was applied. The number of HIV cases prevented with the intervention under evaluation, compared with no intervention, was also reported as an output of the model.

Direct costs
Discounting was relevant since the lifetime costs were estimated. An annual discount rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used, as most of the costs were presented as macro-categories. The health services included in the economic evaluation were antiretroviral therapy, rapid testing and other diagnostic services, counselling, and the lifetime costs of HIV-infected women and HIV-infected infants. The cost/resource boundary of the study was unclear. Both the costs and quantities were estimated using data derived from published studies or hospital accounting systems. Most of the HIV-related data were derived from the AIDS Cost and Service Utilization Survey. The drug costs came from average wholesale prices. Several assumptions about resource use were made. All of the costs were presented in 2000 values using the Consumer Price Index for Medical Care.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs do not appear to have been included.

Currency
US dollars ($).

Sensitivity analysis
Univariate and multivariate sensitivity analyses were performed to examine the robustness of the study results to variations in several model inputs. The model inputs were varied over ranges of values that were mainly derived from...
the literature. Threshold analyses were also performed.

**Estimated benefits used in the economic analysis**

The estimated number of QALYs was not reported. In a cohort of 50,000 women, compared with no intervention, the rapid test followed by prophylaxis resulted in 387 women testing positive for HIV (44% falsely positive) and would prevent 27 cases of HIV.

**Cost results**

In the cohort of 50,000 women, the intervention saved $3 million each year relative to no intervention.

**Synthesis of costs and benefits**

An incremental cost-utility ratio was calculated to combine the costs and benefits of the interventions under evaluation. However, in the base-case, the costs and benefits were not combined because the intervention (rapid test followed by prophylaxis) dominated the option of no intervention, which was both more expensive and less effective (fewer HIV cases prevented).

The analysis of alternative scenarios suggested that nevirapine prophylaxis would be preferred over zidovudine if the relative risk reduction of transmission with nevirapine prophylaxis was at least 0.61. Prophylactic administration to both mother and infant of either nevirapine or lamivudine, in addition to zidovudine, required that the combination be only minimally more effective in comparison with zidovudine monotherapy (relative risk reduction about 0.001 - 0.002 greater) to save additional costs.

With respect to the rapid test, empiric nevirapine therapy would be the preferred strategy over no intervention when rapid testing was not available, the acceptance rate of rapid HIV testing and treatment was 0.68, or the relative risk reduction with nevirapine prophylaxis were somewhat better than with zidovudine (relative risk reduction 0.71 for nevirapine compared with 0.62 for zidovudine prophylaxis). It would also be preferred if all infants were not ruled out for HIV by HIV polymerase chain reaction tests.

The sensitivity analysis showed that the results of the base-case were, in general, quite robust to variations in the base-case model inputs. Variable values had to be relatively extreme to result in the intervention being not cost-effective.

The threshold analysis suggested that the intervention was cost neutral when:

- the acceptance rate of the rapid test was 0.26;
- the proportion of women delivering before treatment was effective was 0.70;
- the prevalence of HIV in women without prenatal care was 2/1,000;
- the relative risk reduction in vertical HIV transmission was 0.25; or
- the additional cost associated with earlier HIV treatment (compared with delayed treatment) was $13,000.

Nevertheless, the intervention remained cost-effective (i.e. it had a cost per QALY below the threshold of $50,000 per QALY).

**Authors’ conclusions**

The strategy of offering the rapid test to all women presenting in labour without prior prenatal care, coupled with antiretroviral prophylaxis for those testing positive, was cost-effective in comparison with no intervention as it prevented the vertical transmission of human immunodeficiency virus (HIV) and saved money. The results of the study showed that whichever prophylactic regimen was the most effective among those recommended in the USA, it would also be the most cost-effective. A strategy of empirical testing where the rapid test was not available was also cost-
CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparator was clear. It represented the standard pattern of care in several settings where no rapid test and subsequent prophylaxis was implemented. You should decide whether this is a valid comparator in your own setting. The authors also considered an alternative strategy to the rapid test and different prophylaxis options.

Validity of estimate of measure of effectiveness
The effectiveness evidence came mainly from published data. However, it was not explicitly stated whether a review of the literature had been undertaken to identify relevant studies. No information on the designs and characteristics of the primary studies was reported. Therefore, it was not possible to assess the validity of the primary sources. The primary studies were combined using a narrative approach and alternative sources of values were used in the sensitivity analysis. Some assumptions were also required in the decision model. In general, the issue of uncertainty due to variability in the data was addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate as it represents a valid measure and is comparable with the benefits of other health care interventions. In addition, it captures the impact of the intervention on both quality of life and survival. Discounting was applied, as recommended in US guidelines for the economic evaluation. However, the estimated number of QALYs was not reported and other model outputs (cases of HIV prevented) were given.

Validity of estimate of costs
The authors stated that a societal perspective was adopted. However, it appears that the indirect costs (i.e. those associated with productivity losses) have not been included in the economic evaluation. Therefore, this limits the perspective used in the study. Only direct medical costs appear to have been included in the analysis. The authors stated that the inclusion of indirect costs would have favoured the intervention strategies. The source of the data was provided. The bulk of the evidence on the costs came from published economic evaluations of HIV-infected individuals and infants; other costs came from hospital databases and market values. A breakdown of the cost items was not clearly presented, which reduces the possibility of replicating the results of the study. The cost estimates were not extensively varied in the sensitivity analysis. The price year was reported, which aids reflation exercises in other settings. Discounting was relevant and was carried out.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies, stating instead that their results corroborated those of published economic evaluations. The issue of the generalisability of the study results to other settings was not explicitly addressed, although sensitivity analyses were carried out on several model inputs. It was noted that the impact of breastfeeding was not incorporated into the decision model.

Implications of the study
The study results suggested that the offer of rapid HIV testing and subsequent preventive treatment to HIV-positive pregnant women without prenatal care, to prevent vertical transmission of the disease, reduced the estimated number of HIV cases and saved costs.

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Other publications of related interest


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