Cost-effectiveness of nevirapine to prevent mother-to-child HIV transmission in eight African countries


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 nevirapine prophylaxis to prevent mother-to-child transmission of the human immunodeficiency virus (HIV). Nevirapine prophylaxis consisted of a single dose to each mother and infant consistent with the HIVNET-012 trial, where mothers who consented to HIV testing and tested positive were offered nevirapine to them and their offspring. The mother was instructed to take her dose of nevirapine at the onset of labour and was then instructed to return at 72 hours after delivery for the baby's dose.

Type of intervention
Primary prevention.

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

Study population
The study population comprised HIV-infected pregnant women seeking antenatal care.

Setting
The setting was antenatal clinics. The economic evaluation was carried out for eight African countries: Botswana, Cote d'Ivoire, Kenya, Rwanda, Tanzania, Uganda, Zambia and Zimbabwe.

Dates to which data relate
The effectiveness evidence was obtained from studies dating from 1993 to 2004. The utilisation and cost data were from 2000 to 2002. The price year was 2000.

Source of effectiveness data
The evidence was derived from a review or synthesis of published studies, augmented by experts' opinions.

Modelling
The model estimated the incremental cost-effectiveness of a short-course nevirapine intervention for HIV-infected pregnant women and their offspring. Field data from intervention programmes from eight sub-Saharan African countries were used to make the model as realistic as possible. The model was then used as a base-case analysis from which to calculate the outcomes. An aggregate stochastic model was developed from the base-case country level models using the highest value, average value and lowest value across country level parameters. Biological and epidemiological values in the stochastic model utilised the point estimates and 95% confidence intervals (CIs) for parameters based on published study results. Triangular probability distribution functions were applied to each of the model parameters with the range of values described. Iterations of the model were conducted until changes in the sampled variable values and...
associated model outcomes changed by less than 1.5% in both the mean and the standard deviation.

**Outcomes assessed in the review**
The parameters obtained from the review included:

the infant HIV infections averted,

the total HIV infections averted,

the adult HIV prevalence rates,

the HIV transmission rates from mother to infant,

the breastfeeding rate, and

drug and treatment efficacy.

It was assumed that no drug-related morbidity or mortality was associated with the regimen examined.

**Study designs and other criteria for inclusion in the review**
No inclusion or exclusion criteria for the studies were reported. A number of primary studies of various designs and meta-analyses of clinical trials were identified and used.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

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

**Number of primary studies included**
The authors reported that approximately 38 studies provided effectiveness evidence.

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

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
For the base-case, the intervention would avert from 243 annual infant HIV infections in Botswana to 2,774 in Tanzania.

The reduction in the adult HIV prevalence rate that would have to be achieved to avert an equivalent number of infant HIV infections as achieved with the nevirapine intervention ranged from 0.89% in Uganda to 4.47% in Botswana.
The equivalent reduction in the number of adult HIV infections averted ranged from 35,134 in Botswana to 252,758 in Tanzania.

The percentage reduction in HIV-infected women becoming pregnant that would achieve an equivalent reduction in infant HIV infections as the nevirapine intervention ranged from 5.63% in Kenya to 34.77% in Rwanda.

Methods used to derive estimates of effectiveness
The analyses were informed by published data, expert opinion and authors’ assumptions.

Estimates of effectiveness and key assumptions
The authors made some key assumptions in the base-case scenario:

- the effectiveness rate for nevirapine was a 47% reduction in mother-to-child transmission;
- the breast feeding rate was 80% among HIV-infected women who were aware of their infection status and transmission;
- no drug-related morbidity or mortality was associated with the regimen examined;
- disease progression parameters were adapted from published data, with 25% of infected infants moving from HIV infections to acquired immune deficiency syndrome (AIDS) within 12 months, 80% by 60 months, and 100% by 120 months;
- mortality from AIDS was estimated to occur within one year of progression to AIDS.

Measure of benefits used in the economic analysis
The measure of benefit used was the disability-adjusted life-years (DALYs). Disability weights for HIV infection and AIDS were estimated to be 0.123 and 0.505, respectively, and were derived from published literature. The number of life-years saved was adjusted to reflect standard age preferences, which gave greater weight to economically productive life-years. The DALYs were discounted at an annual rate of 3% (0% and 6% in the sensitivity analysis).

Direct costs
The costs were for enhancements to the health system to enable the intervention, pre-test counselling, HIV testing and post-test counselling, and nevirapine for the mother and infant. The costs of enhancements to the health system included clerical expenses for record management, infrastructure costs, expenses related to maintaining a drug stock, and expenses for informational leaflets and community education. The costs were adjusted to reflect the intensity of activities at each step in the intervention process and for the size of the programme to reflect resource use. Salaries were also adjusted to generate country-specific estimates.

The averted medical costs for HIV-infected infants were not taken into consideration when calculating the costs of the programme, as there were few data available. However they were considered in the sensitivity analysis using a proxy from another country.

Discounting was carried out at an annual rate of 3% (0% and 6% in the sensitivity analysis). Country-specific data were collected from published sources, while utilisation data came from the UNICEF-supported demonstration project sites. The price year was 2000.

The authors made some assumptions about resource use. For example, the time allocated for post-test counselling was calculated separately for HIV-infected and uninfected clients. For HIV-infected clients, adherence to the US Centers for Disease Control and Prevention's standards for an individual post-test was assumed.

Statistical analysis of costs
The costs were treated stochastically, and a triangular probability distribution function was used for some parameters.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and multivariate sensitivity analyses were conducted. The ranges used were 95% CI values or ranges from published sources. Triangular distributions were assumed for the stochastic analysis.

**Estimated benefits used in the economic analysis**
In the base-case analysis, the DALYs saved were 7,571 in Botswana, 12,984 in Cote d'Ivoire, 18,873 in Zambia, 27,784 in Kenya, 31,462 in Zimbabwe, 39,846 in Uganda, 39,095 in Rwanda and 82,806 in Tanzania.

**Cost results**
The overall programme cost was driven primarily by the population size and the HIV prevalence in each country.

In the base-case analysis, the national programme cost $439,537 in Botswana, $4,026,532 in Cote d'Ivoire, $1,614,182 in Zambia, $3,878,577 in Kenya, $3,620,417 in Zimbabwe, $6,679,675 in Uganda, $2,578,315 in Rwanda and $6,336,391 in Tanzania.

**Synthesis of costs and benefits**
The cost per DALY saved averaged $127 across countries. The most cost-effective programme was in Botswana, with a cost per DALY saved of $58. The least cost-effective programme was Cote d'Ivoire, with a cost per DALY saved of $310.

The intervention cost an average of $123 per DALY saved across iterations of the stochastic model. When all values were set such that they were advantageous to a cost-effective intervention, the result was $13 per DALY saved. Conversely, when all parameters were set to the least advantageous outcome, the cost per DALY saved was $7,627.

In a most likely scenario, modelled by removal of the upper and lower 5th percentile, the cost per DALY saved was $33 at the 5th percentile and $279 at the 95th percentile.

The cost per DALY saved was most sensitive to the mother-to-child transmission rate, with no antiretroviral drug intervention during pregnancy, labour and delivery. Likewise, variation in the probability of mother-to-child transmission of HIV when nevirapine was administered had significant impacts on the outcome. Other model parameters that moderately covaried with the cost per DALY saved included the proportion of women counselled, the estimated lifetime treatment costs for HIV-infected infants, and the costs of HIV testing and post-test counselling.

**Authors’ conclusions**
The most important findings from the analysis were the comparative impact on infant incidence of human immunodeficiency virus (HIV), derived from reducing adult HIV prevalence and reducing unintended pregnancy among HIV-infected women. The authors found that lowering HIV infection rates among sexually active adults by 1 to 5% achieved the same reduction in infant HIV infections as did the nevirapine intervention. By definition, this also resulted in many thousands fewer adult HIV infections and, therefore, must be considered an important cornerstone of a comprehensive package for the prevention of mother-to-child transmission. Similar results were found for the reduction
in unintended pregnancies among HIV-infected women.

**CRD COMMENTARY - Selection of comparators**
The authors gave a justification for the comparators. Recent data suggested that the uptake of counselling, testing and acceptance of antiretroviral drugs might be suboptimal in resource-constrained settings, owing to significant deficits in the ability of health systems to implement the intervention adequately. You should judge whether this prophylaxis intervention is relevant in your own setting, or whether other comparators from other commonly used drugs could also be relevant.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken. Although a more ad hoc review is common practice with models, it does not always ensure that the best data available are used in the model. For this analysis the authors used data from the available studies selectively. In addition, one cannot be sure that all relevant literature was identified, although it is positive that meta-analyses and clinical trials were used to derive the effectiveness measures and that the authors made only a limited number of assumptions. The estimates of effectiveness were derived credibly from the studies identified. The authors used data from published sources, expert opinion and their own assumptions. The effectiveness evidence was derived from a meta-analysis and a randomised clinical trial, which are adequate sources for estimating effectiveness. The authors justified their assumptions with reference to the medical literature. The estimates were investigated in sensitivity analyses, using ranges from the literature, and this will help the external validity of the results obtained. The authors provided a justification for the ranges selected and reported.

**Validity of estimate of measure of benefit**
The authors used DALYs as the measure of benefits. These were derived through modelling. The source from the literature used to derive the disability weights was reported. Sensitivity analyses over adjusted DALYs were conducted and the ranges used were reported.

**Validity of estimate of costs**
The authors reported that the costs were estimated from a programme perspective, thus the indirect costs were appropriately not included. Some costs could have been omitted from the analysis, but these were unlikely to have affected the authors’ conclusions since the intervention costs were underestimated.

To estimate the total direct costs, the authors considered the medical costs and the drug acquisition cost. Although these were taken from published sources, the variation among the different countries in relation to the use of resources might affect the authors’ conclusions, especially since some of the costs were considered globally. Sensitivity analyses of the costs were conducted, but the ranges were selected on the basis of authors’ assumptions.

Discounting was appropriately carried out, and the rates used for clinical and costs outcomes were equal in all countries.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability was addressed by considering the population and countries selected. The authors’ conclusions reflected the scope of the analysis. The authors stated that the principal limitation of the model was related to the use of client data from zidovudine-based programmes, and that the cost of implementation, programme acceptance and nevirapine use might vary across the countries. Zidovudine is used in Botswana, Cote d'Ivoire, Zambia and Zimbabwe, while zidovudine and nevirapine are used in Kenya, Rwanda, Tanzania and Uganda. No differences in trends were found when the two groups were compared. Likewise, in a study of women attending antenatal clinics in 13 countries in Africa, it was found that acceptance and return rates for HIV testing did not depend on the antiretroviral interventions delivered.
Implications of the study
Efforts must be made to simplify the process of providing HIV counselling and testing and associated antiretroviral prophylaxis to eligible women. Significant financial resources would be needed to achieve these goals, but such investments would have multifaceted benefits, including improvements in basic antenatal services. Increased access to HIV counselling and testing would also allow HIV-infected mothers to make informed decisions. The efficacy of the nevirapine regimen was much lower than desired. Programmes could spend up to $152 per women on an antiretroviral drug that had 70% efficacy and would achieve the same cost-effectiveness as the nevirapine programme.

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