Economic impact of treatment of HIV-positive pregnant women and their newborns with zidovudine

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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
Zidovudine, ante-partum and intra-partum maternal therapy and 6 weeks of neonatal therapy, to reduce the maternal-infant transmission rate of the human immunodeficiency virus (HIV).

Type of intervention
Treatment and primary prevention

Economic study type
Cost-effectiveness analysis.

Study population
HIV-positive pregnant women and their newborns.

Setting
The practice setting was the hospital. The economic study was carried out in North Carolina, USA.

Dates to which data relate

Source of effectiveness data
Effectiveness data were derived from a single study (Connor, 1994).

Link between effectiveness and cost data
Costing was undertaken on a hypothetical sample of patients, using cost estimates from the published literature.

Study sample
477 HIV-infected, pregnant women, who were eligible and who consented, were enrolled in the study. The number of eligible women who refused to participate was not reported. The study patients were all between 14 and 34 weeks’ gestation and had no indication for antiretroviral therapy. 239 women were randomised to the zidovudine group and 238 received placebo. The median age of women in both groups was 25 years. Of the zidovudine group 20% were white, 45% were black and 30% were Hispanic. The placebo group comprised 16% white, 53% black and 26% Hispanic. The median CD4 cell count (cells/mm$^3$) was 360 in the zidovudine group and 538 in the placebo group. The median gestational age at entry was 26 weeks in the zidovudine group, compared with 27 weeks in the placebo group. 17% of the zidovudine group and 15% of the control group had a history of injection drug use. 22% of the intervention group and 21% of the placebo group had a sexually transmitted disease. The use of power calculations was not reported.
Study design
The study was of a double blind, placebo-controlled, randomised design, and was based in 59 centres located in France and the USA. Women were stratified according to gestational age and then randomly assigned to receive placebo or zidovudine, consisting of ante-partum oral treatment, intra-partum intravenous treatment and 6 weeks of oral neonatal therapy. Mothers were followed up for 6 months postnatally, whilst infants were followed up until 78 weeks of age. 59 women (25%) were lost to follow up in the zidovudine group and 55 (23%) in the control group. The main reasons for loss to follow up were that women were still pregnant at the time of analysis (24 in both groups) and that culture data were unavailable for the infant (25 in the zidovudine group and 21 in the control group). Other reasons included no confirmed HIV infection, withdrawal before pregnancy and loss of pregnancy.

Analysis of effectiveness
The analysis of effectiveness was based on treatment completers only and included 363 deliveries of live infants, 180 of these being in the zidovudine group. The primary health outcome was the maternal-infant transmission rate. Groups were shown to be comparable in terms of demographic and clinical characteristics.

Effectiveness results
13 (7.2%) infants in the zidovudine group had at least one positive HIV culture, compared with 40 (21.9%) infants in the placebo group. Using the Kaplan Meier analysis, the estimated proportion of infants infected at 18 months was 8.3% (95% CI: 3.9 - 12.8%) for the zidovudine group and 25.5% for the control group (95% CI: 18.4 - 32.5%). This difference was statistically significant (Z=4.03, p=0.00006) and corresponds to a relative reduction in the risk of HIV transmission of 67.5% (95% CI: 40.7 - 82.1%). 24 women (13%) in the placebo group and 26 women (14%) in the zidovudine group experienced adverse effects, all of which were judged to be related to labour and delivery.

Clinical conclusions
In pregnant women with mildly symptomatic HIV disease and no prior treatment with antiretroviral drugs during the pregnancy, zidovudine given ante-partum and intra-partum to the mother and to the newborn for 6 weeks reduced the risk of maternal-infant HIV transmission by approximately two-thirds.

Modelling
A simple decision tree model was used to find the expected cost of each treatment arm, by combining the estimate of efficacy for zidovudine with cost estimates, and estimates of paediatric morbidity. The model was also used to conduct a range of sensitivity analyses. The efficacy estimate was derived from a Kaplan-Meier survival analysis.

Measure of benefits used in the economic analysis
The benefit measure was cases of perinatal HIV transmission.

Direct costs
The cost boundary adopted was that of the hospital. The analysis included the cost of zidovudine, the cost of laboratory tests and the cost of treating paediatric HIV infection. The latter included the cost of hospital days, emergency department visits, other ambulatory care visits, home care visits, dental visits and HIV-related prescription drugs. Costs and quantities were not reported separately, except for zidovudine: the unit cost of the drug came from average wholesale prices. The cost of laboratory tests was based on an assumption. The cost of treating paediatric HIV infection was taken from the medical literature. The annual charge estimate was first converted to a cost estimate, then converted to 1994 dollars and finally converted to a weighted average lifetime cost. In the baseline analysis, costs were not discounted. The cost of administering zidovudine therapy and laboratory tests, the cost of informal care and the cost of treating adverse effects were not included in the analysis.
Statistical analysis of costs
Not applicable.

Indirect Costs
Not included.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were performed, in which 3 estimates were varied independently. These included the perinatal transmission rate, the cost of zidovudine, and the treatment cost for paediatric HIV (reflecting variations in the proportion of HIV-positive infants with rapidly progressive disease and the duration of each stage for those who progress later). An analysis of extremes was also conducted on these variables, to represent a ‘worst case’ scenario. A threshold analysis was conducted to determine the combinations of paediatric lifetime cost and efficacy rate for which the intervention would be cost-neutral. Finally, the effect on savings of introducing a discount rate was explored.

Estimated benefits used in the economic analysis
In hypothetical cohorts of 100 HIV-positive pregnant women, it was estimated that 8.3 infants in the zidovudine group and 25.5 infants in the control group would be HIV-positive.

Cost results
In the baseline analysis, the mean cost per woman-infant pair was estimated to be $92,549 for the zidovudine group and $252,233 for the control group. In a cohort of 100 women, this would result in total cost savings of $1,596,831 attributable to treatment with zidovudine. Varying the cost of zidovudine treatment had little effect on cost savings. However, savings were found to be sensitive to changes in lifetime paediatric treatment costs and to assumptions regarding the efficacy rate of zidovudine. In a one-way analysis, cost savings were found to be positive, if the transmission rate in the treatment group were assumed to be 24.4% or less. In the worst case scenario in which all three variables were changed simultaneously, savings fell to $523,380, representing 33% of the baseline value. The threshold analysis revealed that at low levels of lifetime paediatric treatment costs, zidovudine was still cost saving for a wide range of efficacy rates. Increasing the discount rate was found to lower the level of savings achieved.

Synthesis of costs and benefits
Since the intervention was found to be cost saving, a synthesis of costs and benefits was unnecessary.

Authors’ conclusions
Cost savings from the treatment of HIV-positive women and their babies are achieved for a wide range of possible maternal treatment costs, efficacy rates and lifetime paediatric treatment costs.

CRD COMMENTARY - Selection of comparators
The choice of comparator, no antiretroviral treatment, was chosen to represent usual practice. You, the user of the database, should decide if this is applicable in your own setting.

Validity of estimate of measure of effectiveness
The measure of efficacy, the perinatal transmission rate, was derived from a randomised-controlled trial of women with mildly symptomatic HIV disease. Although the effect of other factors on the transmission rate, such as breast-feeding and caesarean section, was not formally investigated, the impact on cost savings of varying the estimate of efficacy was
considered by means of a sensitivity analysis.

**Validity of estimate of costs**
The estimates related to the US setting. Variations in treatment costs outside the USA were not explicitly explored, although sensitivity analyses were conducted to investigate the impact of variations in the cost of zidovudine treatment and of lifetime paediatric treatment. Nevertheless, it is possible that, outside the US setting, both these costs could vary beyond those ranges explored in the sensitivity analysis. The implications for cost savings in these settings should therefore be interpreted with caution.

**Other issues**
The study also investigated, by means of a decision tree model, the cost-effectiveness of introducing a voluntary screening programme for women of unknown HIV status. Under baseline estimates, the programme would be cost saving if HIV prevalence rates in the screened population were between 5 and 50 per 1,000. The impact of changes in a wide range of estimates, including HIV prevalence, screening acceptance rate, the sensitivity and specificity of the tests, and cost and efficacy estimates, were explored by sensitivity analyses. When applied to the US population, the cost per case of perinatal HIV transmission averted was estimated to be in the range of $154,461 to $184,423. The authors concluded that such programmes would enhance the cost savings and health benefits of zidovudine, particularly if populations with high HIV prevalence were targeted.

**Implications of the study**
Further research addressing the mechanism by which zidovudine reduces the risk of perinatal transmission and the role of other risk-reducing mechanisms, such as delivery by caesarean section, are needed to give a more accurate estimate of the cost-effectiveness of zidovudine.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
8656505

**Other publications of related interest**
Details of the effectiveness measure reported in this abstract were taken from the following publication:


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
AIDS Serodiagnosis /economics; Abortion, Induced; Antiviral Agents /economics /therapeutic use; Cost Savings; Cost of Illness; Counseling /economics; Drug Costs; Female; HIV Infections /economics /prevention & control /transmission; HIV Seropositivity /drug therapy /economics /transmission; HIV Seroprevalence; Health Care Costs /statistics & numerical data; Humans; Infant, Newborn; Infectious Disease Transmission, Vertical /economics /prevention & control; Mass Screening /economics; Pregnancy; Pregnancy Complications, Infectious /drug therapy /economics /prevention & control; Pregnant Women; Sensitivity and Specificity; United States /epidemiology; Voluntary Programs; Zidovudine /economics /therapeutic use