Prevention of mother-to-child transmission of HIV-1 infection: alternative strategies and their cost-effectiveness

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 intervention strategies to reduce mother-to-child transmission of human immunodeficiency virus (HIV). The four strategies were:

bottle-feeding instead of breast-feeding;
bottle-feeding plus elective Caesarean section (CS) delivery;
bottle-feeding plus giving zidovudine (ZDV) to the mother antenatally, during labour and to the baby for the first 6 weeks of life; and
bottle-feeding plus ZDV plus elective CS.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The patient population comprised HIV-positive pregnant women whose HIV status was known.

Setting
The setting was secondary care. The economic study was conducted in the United Kingdom.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a review of published results.

Modelling
A decision tree model was used to estimate the overall transmission risk and cost associated with each strategy.
Outcomes assessed in the review
The following outcomes were assessed in the literature review:

the odds ratio (OR) of transmission for elective CS versus other modes of delivery (emergency CS and vaginal),

the proportion of infections that occurred in utero,

the difference in transmission rates between bottle- and breast-fed babies,

the efficacy of ZDV, and

the uptake rates of bottle-feeding, elective CS and ZDV in the UK among women who were and were not aware of being HIV-positive.

Study designs and other criteria for inclusion in the review
The authors stated that the OR for elective CS versus other modes of delivery was taken from a large prospective study. The difference in transmission rates between bottle- and breast-fed babies was taken from a meta-analysis. The efficacy of ZDV was taken from a clinical trial. No details were given about the other studies from which the data were derived.

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
Eleven studies were included in the review.

Methods of combining primary studies
The OR for elective CS versus other modes of delivery was taken from a single study, because other studies grouped elective and emergency CS together. The proportion of infections that occurred in utero was derived by taking a weighted average of the results from two studies. All other data were derived from a single source for each item.

Investigation of differences between primary studies
See the previous field.

Results of the review
The review generated the following results:

the adjusted OR for elective CS versus other modes of delivery was 0.594 (95% confidence interval, CI: 0.36 - 0.98);

the proportion of infections that occurred in utero was 0.338 (95% CI: 0.26 - 0.42);

the difference in the transmission rates between bottle- and breast-fed infants was 14% (95% CI: 7 - 22);
ZDV reduced transmission by a factor of 3.072 (95% CI: 1.69 - 5.59); there was a 96% uptake of bottle-feeding, 44% uptake of elective CS, and 75% uptake of ZDV among women who were aware of being HIV-positive during pregnancy; and there was a 34% uptake of bottle-feeding, 6% uptake of elective CS, and 0% uptake of ZDV among women who were unaware of being HIV-positive during pregnancy.

These data were used to derive the transmission risk parameters by solving 5 equations for 5 unknowns.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions in constructing their model.

**Estimates of effectiveness and key assumptions**
ZDV was assumed to reduce the risk of transmission by the same factor in utero, during delivery and after delivery. To convert the effectiveness data into model parameter estimates, it was assumed that 10% of women would choose elective CS and that 10% of mothers breast-feed.

**Measure of benefits used in the economic analysis**
The benefit measure used was the vertical HIV transmissions avoided.

**Direct costs**
The health service costs included in this analysis were for ZDV therapy, the delivery and bromocriptine, a drug that suppresses milk production. The costs of ZDV therapy included the drugs themselves and their administration antenatally for the average duration of 11 weeks, during labour and to the infant for the first 6 weeks of life. The costs of staff time for counselling women about breast-feeding were excluded on the grounds that counselling is given to all pregnant women. The patient costs of bottle-feeding (bottles and equipment) were also excluded.

The resource use and the costs were derived from sources published between 1991 and 1996, and from discussions with a London maternity unit (for the cost of administering ZDV during delivery). Where necessary, the costs were adjusted to 1996 prices using the NHS price inflation index. Discounting was irrelevant as the prevention strategies were carried out within a one-year period.

**Statistical analysis of costs**
The costs were treated as point estimates.

**Indirect Costs**
The indirect costs were not included in this analysis.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
The authors examined three scenarios.

The base-case assumed a 100% uptake of bottle-feeding, ZDV and CS.

The second scenario examined the effects of incomplete uptake of the interventions, using national estimates, which
thus provided an analysis from a public health perspective.

The third scenario consisted of two one-way sensitivity analyses exploring the impact of uncertainty over CS uptake and ZDV uptake, respectively.

**Estimated benefits used in the economic analysis**

From a clinical or individual woman perspective, the estimated transmission risks were:

31.6% (95% CI: 23.8 - 39.3) if no measures were taken,

17.7% (95% CI: 15.5 - 19.9) for bottle-feeding alone,

11.3% (95% CI: 7.1 - 17.7) for bottle-feeding plus elective CS,

5.8% (95% CI: 3.1 - 10.6) for bottle-feeding plus ZDV, and

3.7% (95% CI: 1.7 - 7.8) if all three measures were used.

From a public health perspective, the equivalent estimated transmission risks were:

26.5% (95% CI: 21.1 - 31.9) if no measures were taken,

17.9% (95% CI: 15.7 - 20.1) for bottle-feeding alone,

15.5% (95% CI: 12.9 - 18.8) for bottle-feeding plus elective CS,

8.8% (95% CI: 6.7 - 12.7) for bottle-feeding plus ZDV, and

7.6% (95% CI: 5.6 - 11.3) if all three measures were used.

**Cost results**

From a clinical point of view, taking no measures resulted in an estimated cost of 466.70 per woman (that is, the cost of a non-elective CS delivery).

The expected cost of bottle-feeding only was 468.80.

The cost of bottle-feeding plus elective CS was 1,054.10.

The cost of bottle-feeding plus ZDV was 1,382.80.

The cost of using all three measures was 1,968.10.

The corresponding expected per woman costs from a public health point of view were:

502.50 if no measures were taken,

503.80 for bottle-feeding only,

726.20 for bottle-feeding plus elective CS,

1,189.30 for bottle-feeding plus ZDV, and

1,411.70 if using all three measures.
Synthesis of costs and benefits
The results were combined in the form of an incremental cost per transmission avoided. The more expensive strategies
were compared with the next cheaper strategy in an incremental analysis.

From a clinical point of view:
- compared with no intervention, bottle-feeding only has an incremental cost-effectiveness ratio (ICER) of 15;
- compared with bottle-feeding only, bottle-feeding plus elective CS has an ICER of 9,186;
- compared with bottle-feeding plus elective CS, bottle-feeding plus ZDV has an ICER of 7,658; and
- compared with bottle-feeding plus ZDV, using all three measures has an ICER of 27,836 in 1996 prices.

From a public health point of view, the corresponding ICERs were:
- 15 for bottle-feeding only;
- 9,248 for bottle-feeding plus elective CS, compared with bottle-feeding only;
- 7,594 for bottle-feeding plus ZDV, compared with bottle-feeding plus elective CS; and
- 18,546 using all three measures, compared with bottle-feeding plus ZDV.

The authors also analysed how the ICERs of particular strategies changed with changes in the uptake of the other
prevention measure. For example, the ICER of bottle-feeding plus elective CS ranged from 9,248 at 0% uptake of
ZDV, to 27,895 at 100% ZDV uptake. Similarly, the ICER of ZDV ranged from 7,437 at 0% uptake of CS, to 11,342
at 100% uptake of CS.

Authors’ conclusions
Comparing the incremental cost-effectiveness ratios (ICERs) with the estimated lifetime cost of caring for a human
immunodeficiency virus (HIV)-positive child, the authors concluded that, in addition to encouraging bottle-feeding, the
use of zidovudine (ZDV) appears to be cost-effective under a wide range of situations. The cost-effectiveness of
elective Caesarean section (CS) was subject to more uncertainty, due to a lack of data, and may not be cost-effective
when the uptake of ZDV is high.

CRD COMMENTARY - Selection of comparators
The authors stated that the strategies were compared with a "do-nothing" alternative, in order to estimate their cost-
effectiveness relative to the risk that would exist if no measures were taken. You must decide if this is a relevant
comparator in your own setting. This decision depends on whether or not routine preventative measures are already
undertaken in your setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review was carried out, although the sources used appear to have been of
good quality. Where more than one estimate for a parameter was found, the authors took a weighted average.

Validity of estimate of measure of benefit
The authors used a condition-specific benefit measure, which limits the comparability of their findings with those in
other disease areas. Thus, the cost-effectiveness of HIV transmission-reduction strategies cannot be compared with
other uses of hospital resources. The authors recommend further research to develop a generic outcome measure in this
area. However, the cost per transmission prevented measure is useful in that it can be directly compared with estimates
of the (discounted) lifetime cost of caring for a child who has HIV.
Validity of estimate of costs
The relevant cost components were included in the analysis. The authors excluded the cost of counselling women about breast-feeding, as all women are routinely provided with such counselling. Some may argue that this counselling might be more intense with HIV-positive women. The resource use was not reported separately, but it is likely that some of these data could be obtained from the primary sources used in the cost analysis.

Other issues
The model was well described in a short appendix and, therefore, should be reproducible in other settings. Moreover, the authors addressed the issue of generalisability of the cost data, and suggested how their ICERs could be adapted to cost differences in other countries. The authors did not compare their results with those in the literature. They made a number of recommendations that seem justified, given the scope of their analysis.

Implications of the study
Due to the uncertainty surrounding the cost-effectiveness of CS, the authors recommend more research on the efficacy of elective CS as opposed to other modes of delivery. They also recommend more research to ascertain whether ZDV is more effective at some points in the perinatal period than in others. Additionally, the authors recommend an increase in the rate of identifying HIV-positive women in pregnancy through antenatal screening.

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Other publications of related interest


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