The cost-effectiveness of elective Cesarean delivery for HIV-infected women with detectable HIV RNA during pregnancy

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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 authors compared elective Caesarean section for HIV infected women with detectable HIV RNA at 38 weeks gestation with vaginal delivery at term. No further details are given.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The population consisted of hypothetical pregnant HIV-infected women with detectable HIV RNA levels, and their offspring.

Setting
The study was based on the treatment of hypothetical patients; therefore a setting was not explicitly stated. However, as vaginal delivery and Caesarean section generally occur within a hospital setting the setting can be assumed to be secondary care.

Dates to which data relate
The effectiveness data were taken from studies published between 1977 and 1999. Cost data were taken from published sources dating between 1995 and 1998.

Source of effectiveness data
The effectiveness data were taken from a review and synthesis of previously completed studies, supplemented with some authors’ assumptions.

Modelling
A probabilistic decision-analytic model was used to calculate the cost and quality-adjusted life expectancy of the two delivery strategies.

Outcomes assessed in the review
Outcomes assessed in the review were as follows:

Delivery rates: probability of vaginal delivery under the vaginal delivery strategy; probability of Caesarean delivery
under the vaginal delivery strategy; probability that Caesarean section is urgent under the vaginal delivery strategy; probability of vaginal delivery under the elective Caesarean strategy; probability of Caesarean delivery under the elective Caesarean strategy; probability that Caesarean section is urgent under the elective Caesarean strategy.

Maternal morbidity and mortality rates: mortality from vaginal delivery (per 100,000 deliveries); relative risk of death with urgent Caesarean section; relative risk of death with elective Caesarean section; complication rate with vaginal delivery; relative risk of complications with Caesarean section.

Vertical transmission rates: with vaginal delivery (percentage); relative risk of transmission with non-elective Caesarean section; relative risk of transmission with elective Caesarean section.

Study designs and other criteria for inclusion in the review
The authors did not report that they carried out a systematic review of the relevant literature, and did not report the inclusion and exclusion criteria for the studies included. Delivery rates were taken from a randomised trial. The authors did not report the study designs of the sources for the mortality data, vertical transmission rates, and complication rates.

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
Sixteen primary studies were included in the review of effectiveness data.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
In some cases the authors reported differences between outcomes presented in primary studies. Explanations for these differences were suggested. For example, vertical transmission rates were reported to differ due to rates being stratified in one study and not in another. The authors explored the impact of such differences using sensitivity analysis.

Results of the review
Values in parentheses were used in the sensitivity analyses.

Delivery rates:

Probability of vaginal delivery under the vaginal delivery strategy, 0.73 (0.7 - 0.85);
Probability of Caesarean delivery under the vaginal delivery strategy, 0.27 (0.15 - 0.3);
Probability that Caesarean section is urgent under the vaginal delivery strategy, 0.54 (0 - 1);
Probability of vaginal delivery under the elective Caesarean strategy, 0.12 (0.05 - 0.25);
Probability of Caesarean delivery under the elective Caesarean strategy, 0.88 (0.15 - 0.28 - this appears to be a transcription error);

Probability that Caesarean section is urgent under the elective Caesarean strategy, 0.05 (0 - 0.2).

Maternal morbidity and mortality rates:

Mortality from vaginal delivery (per 100,000 deliveries), 7.8 (1.1 - 9.8);

Relative risk of death with urgent Caesarean section, 4.2 (1 - 11.5);

Relative risk of death with elective Caesarean section, 1.9 (1 - 4.2);

Complication rate with vaginal delivery, 0.17 (0 - 0.4);

Relative risk of complications with Caesarean section, 2.5 (1 - 5).

Vertical transmission rates:

With vaginal delivery (percent), 6.7 (0 - 41);

Relative risk of transmission with non-elective Caesarean section, 1.0 (0.4 - 2);

Relative risk of transmission with elective Caesarean section, 0.43 (0 - 1).

**Methods used to derive estimates of effectiveness**

The authors made some assumptions to supplement their literature review.

**Estimates of effectiveness and key assumptions**

The following assumptions were made:

Women with HIV/AIDS had the same delivery-specific mortality rates as uninfected women;

Vertical transmission rates were dependent on the presence of detectable HIV RNA in the mother regardless of antiretroviral regimen;

The HIV transmission rate with vaginal delivery was constant;

The highest morbidity rates were applicable.

**Measure of benefits used in the economic analysis**

Quality-adjusted life expectancy (QALE) was used for the mother and for the child, but was not combined with the cost estimate. The valuation of health states was taken from a published study that reported utilities and life expectancy. Details of the valuation method were not reported. Some of the authors’ assumptions, such as Caesarean section being equivalent to a loss of one week of life, were made to supplement the data from the published study. In addition the authors estimated the number of HIV transmissions and the number of maternal deaths per 1,000 deliveries from the two birth strategies.

**Direct costs**

A societal perspective was adopted for the cost analysis and costs were discounted at a rate of 3%. As the horizon for the study extended over many years (according to the life expectancy of the mother and the child), discounting was necessary. The authors did not report quantities and costs separately.
The following costs (source) were estimated:

- Annual cost estimates for HIV-infected children (AIDS Cost and Service Utilization Survey);
- Drug costs (Red Book);
- Dispensing costs (published study);
- Costs associated with viral load testing (published study);
- Costs of both types of delivery (based on costs at an urban teaching hospital).

Costs for each type of delivery were estimated with and without complications. Costs appear to be based on actual data, although it is not clear whether costs taken from published studies were taken from actual data in the original study. Costs were inflated to 1997 dollars using the Consumer Price Index for medical care. Cost data were obtained from material published between 1995 and 1998. Some 'costs' were adjusted, for instance to convert charges to costs using a cost-to-charge ratio. Details of the conversion were stated clearly.

**Statistical analysis of costs**

No statistical analysis of costs was reported.

**Indirect Costs**

Although the authors stated that they had adopted a societal perspective, they did not account for the time costs of the patients. The authors acknowledged this problem. Given the time implications, particularly of Caesarean section and possible complications, time costs are a potentially relevant factor. The authors did not provide any details of costs included that might otherwise be classified as indirect costs.

**Currency**

Costs were estimated in US dollars ($).

**Sensitivity analysis**

Univariate and multivariate sensitivity analyses were carried out. The authors reported that the reason for the sensitivity analysis was to "assess the stability of the results to the underlying data and assumptions". The ranges used in the effectiveness data are reported above.

Quality adjusted life expectancy:

- Quality-adjusted Life Years (QALYs) for infant infected with HIV, 6.8 - 24.8;
- QALYs for mother if she survives delivery, 4.6 - 22.9;
- Disutility (quality adjusted weeks) for delivery complications, 0 - 13*;
- Disutility (quality adjusted weeks) for Caesarean section, 0 - 13*;

*Note: there is some difference in the reporting of the disutility figures in the paper. The figures given here are taken from Appendix II.

Costs:

- Cost for infant infected with HIV, $92,500 - $416,000;
Cost for vaginal delivery, $1,500 - $6,000;
Cost multiplier for urgent Caesarean, 1.4 - 3;
Cost multiplier for elective Caesarean, 1 - 2;
Cost multiplier for complications, 1 - 2.
Discount rate, 0 - 10%.

The sensitivity analysis seemed to be aimed at investigating variability in the available data rather than improving the generalisability of the study.

**Estimated benefits used in the economic analysis**
The number of births was used in the economic analysis to estimate the cost per birth. The number of births was not reported separately. The following outcomes were reported and could be used by the reader to calculate alternative estimates of benefit:

- the number of HIV transmission per 1,000 deliveries from elective Caesarean was 34.9, and from vaginal delivery was 62.3;
- the number of maternal deaths per 100,000 deliveries from elective Caesarean was 14.7, and from vaginal delivery was 12.3;
- the combined quality-adjusted life expectancy for mother and child from elective Caesarean section was 38.7 years, and from vaginal delivery was 38.2 years.

**Cost results**
The costs were only reported in a combined format as costs per birth for each of the treatment alternatives. Please refer to the synthesis of costs and benefits section below.

**Synthesis of costs and benefits**
The cost per birth for elective Caesarean was reported to be $10,600 ($4,500 in delivery costs plus $6,100 in discounted future medical costs).

The cost per birth for vaginal delivery was reported to be $14,500 ($3,600 in delivery costs plus $10,900 in discounted future medical costs).

Future costs were discounted at 3%.

Elective Caesarean was reported to cost $3,900 less per birth than vaginal delivery.

Costs were estimated both with and without complications. It is not clear if those reported were including or excluding complications.

The authors reported that Caesarean delivery was more effective and less costly over a wide range of assumptions. The HIV transmission rate with vaginal delivery and the relative risk of HIV transmission with elective Caesarean delivery were, however, found to affect the conclusions.

Vaginal delivery dominated (was more effective and less costly) when the vaginal transmission rate was 0 - 0.002 and when the Caesarean transmission rate was 0.98 - 1.

Caesarean delivery gave more QALYs but cost more when the vaginal transmission rate was 0.002-0.013 and when the
Caesarean transmission rate was 0.89-0.98.

Caesarean delivery dominated (was more effective and less costly) when the vaginal transmission rate was 0.013-1.0 and when the Caesarean transmission rate was 0.0-0.89.

Authors' conclusions
The authors concluded that "over a broad range of values and several conservative assumptions biasing the results in favour of the vaginal delivery strategy, the elective Caesarean strategy was associated with increased quality-adjusted life expectancy and lower costs compared with the vaginal strategy". The authors supplemented their comments with examples of how many cases of pediatric HIV infection would be averted per year, how much money might be saved in the USA each year, and how many maternal deaths would be faced over a period of years, with the use of elective Caesarean section.

CRD COMMENTARY - Selection of comparators
The authors compared Caesarean section with vaginal delivery. The comparator (vaginal delivery) was appropriate for the study question, and is the only possible comparator. The authors justified their choice to study Caesarean section and vaginal delivery through a discussion of the controversy surrounding the use of Caesarean section despite its demonstrated benefits.

Validity of estimate of measure of effectiveness
Effectiveness data came from a review of published literature. The authors did not state that they were carrying out a systematic review and did not report their methods for identifying relevant literature. Nevertheless they found many papers relevant to their study. Data from primary studies were used selectively, but with appropriate discussion as to why a particular source was used in preference to another. Sensitivity analysis was appropriately used to explore the differences between primary studies. The authors used some assumptions to supplement data from primary studies. These were generally made to overcome a lack of available data. The impact of some assumptions was explored in sensitivity analysis.

Validity of estimate of measure of benefit
The authors estimated QALYs, the number of maternal deaths and the number of HIV transmissions as measures of benefit. In addition, the authors used the number of births to estimate economic benefit, although this statistic was not reported separately from costs (i.e. the cost per birth was reported). The choice of benefit measure, and other possible benefit measures, was not discussed in detail. For instance, it would have been useful to have compared the cost per HIV-infected child and cost per healthy child, resulting from the alternative delivery methods.

Validity of estimate of costs
Patients' time costs were not included in the analysis despite the fact that the authors explicitly stated that they had adopted a societal perspective. The authors acknowledge this limitation in the study and they explain that including them would have further increased the case for Caesarean section due to the amount of time involved in providing care for an HIV-infected child. Whilst this is possible, there may be other influences (not acknowledged by the authors), which might not improve the case for Caesarean. For instance, mothers delivering by Caesarean section may have to use more time during delivery, and in the event of complications. This influence may increase the cost of Caesarean section. The authors discussed a variety of costs relevant to birth, including immediate delivery costs and longer term care costs. Costs (and benefits) were appropriately discounted. Unit costs were not reported separately from quantities. Separate reporting might have increased the reader's understanding of the decision problem.

Other issues
The authors provided a useful comparison of their results with those from previous studies. The authors discussed some differences between the methodologies of studies, but suggested that the results were consistent. The issue of
generalisability was not discussed. However, extensive sensitivity analysis was carried out exploring a range of values for both efficacy and cost variables. The authors do not appear to have reported their results selectively. The conclusions drawn accurately reflected the design of the study and the results presented. The limitations of the study were presented and discussed by the authors. These included a lack of evidence about whether women receiving highly active antiretroviral therapy (HAART) with comparable HIV RNA would have the same transmission rates as those used in this study.

**Implications of the study**
The authors advised that Caesarean section should be offered to HIV-infected pregnant women with detectable HIV RNA to decrease the probability of mother-to-child HIV transmission. They argued that the decision problem should be reinvestigated as new information, such as transmission rates with combination therapy, becomes available.

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**Other publications of related interest**


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