The cost-effectiveness of elective Cesarean delivery to prevent hepatitis C transmission in HIV-coinfected women

Schackman B R, Oneda K, Goldie S J

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 elective Caesarean delivery (C-section) to prevent perinatal transmission of hepatitis C virus (HCV) in human immunodeficiency virus (HIV)/HCV-coinfected women with suppressed HIV RNA but detectable HCV RNA.

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of pregnant HIV/HCV-coinfected women with suppressed HIV RNA but detectable HCV RNA.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was derived from studies published between 1993 and 2003. The dates for the resource use data were not explicitly reported. The price year was 2003.

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 examine the benefits and costs associated with recommendations for elective C-section (RCS), compared with standard care (SC), for the prevention of perinatal transmission of HCV. The structure of the model was reported. The time horizon of the model appears to have been lifetime. Eligible women could accept or refuse elective C-section, and then undergo vaginal delivery, or urgent or elective C-section. Both maternal and infant complications were considered.

Outcomes assessed in the review
The outcomes assessed from the literature were:

the probabilities of vaginal delivery, elective C-section, and urgent C-section under SC and under RCS;
the rates of maternal morbidity with vaginal delivery, elective C-section, and urgent C-section;
the rates of maternal mortality with vaginal delivery, elective C-section, and urgent C-section;
the vertical transmission rates with vaginal delivery, elective C-section, and urgent C-section; and
the acceptance of RCS.

The utility weights used to calculate quality-adjusted life-years (QALYs) were also estimated from the literature.

Study designs and other criteria for inclusion in the review
A systematic review of the literature does not appear to have been carried out. The authors described the design and main characteristics of the majority of studies used to extrapolate the parameters of the model. In particular, the probabilities of different modes of delivery were taken from a randomised controlled trial, the maternal morbidity rates were obtained from a cohort study, the vertical transmission rate were from a retrospective analysis, and the acceptance of recommendations for C-section were from a pilot study.

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
Nine primary studies were the main source of evidence.

Methods of combining primary studies
The primary studies were combined using a narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
Under SC, the probability of vaginal delivery was 73.2% (range: 66.7 - 78.8), elective C-section 12.3% (range: 8.4 - 17.5), and urgent C-section 14.5% (range: 10.3 - 20.1). The corresponding values under RCS were 11.7% (range: 7.6 - 17.4), 84% (range: 77.8 - 88.8), and 4.3% (range: 2 - 8.5), respectively.

The rate of maternal morbidity was 10.8% (range: 8.8 - 13.1) with vaginal delivery, 26.7% (range: 16.2 - 40.5) with elective C-section, and 32% (range: 24.7 - 40.2) with urgent C-section.

The rate of maternal mortality was 0.0078 (range: 0.0011 - 0.0098) with vaginal delivery. The relative risk for maternal mortality was 4.2 (range: 1.0 - 11.5) with elective C-section relative to vaginal delivery, and 1.9 (range: 1.0 - 4.2) with urgent C-section relative to vaginal delivery.

The vertical transmission rate was 17.3% (range: 13.5 - 22) with vaginal delivery, 8.2% (range: 4.6 - 13.9) with elective
C-section, and 8.2% (range: 4.6 - 13.9) with urgent C-section.

The acceptance of the RCS was 81% (range: 5 - 100).

The discounted quality-adjusted life-expectancy (QALE) was 28.7 years for a healthy infant, 18.2 years for infants that developed chronic HCV as an adult, and 7.6 years (range: 3.8 - 11.4) for HIV-HCV-coinfected mothers surviving delivery.

The complications disutility and C-section disutility for mothers were both 0.02 (range: 0 - 0.23), namely the loss of 1 week in a lifetime.

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
It was conservatively assumed that vertical transmission of HIV did not occur with or without C-section. In addition, antiretroviral therapy had no impact on the outcomes.

Measure of benefits used in the economic analysis
The summary benefit measure used was the number of QALYs associated with each alternative preventive strategy. An annual discount rate of 3% was applied. The QALYs were calculated using the decision model. Other model outputs were the number of perinatal transmission avoided, the maternal deaths per 100,000 deliveries, and the maternal deaths per 1,000 transmissions avoided.

Direct costs
Discounting was relevant, and an annual discount rate of 3% was applied as the lifetime costs were evaluated. The unit costs were not presented separately from the quantities of resources used. The health services included in the economic evaluation were all the hospital costs related to vaginal delivery and C-section, with and without complications. Non-obstetric costs were not considered because they were assumed to have been unaffected by the RCS. The authors stated that the cost/resource boundary of society was adopted. However, only the costs relevant to the service provider appear to have been considered. The costs were derived from the University Health System Consortium, while physician costs were derived from the Medicare physician fee schedule. The source of the resource use data was not reported. The price year was 2003.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out to investigate the issue of robustness of the estimated cost-utility ratios to variations in some model inputs. The inputs investigated included, for example, HCV transmission rates, rate of maternal acceptance of RCS, and the probability of mode of delivery. A Monte Carlo simulation was also performed,
using 1,000 iterations to undertake a multivariate probabilistic sensitivity analysis. Most of the ranges used in the analysis were derived from the literature and were varied around the 95% confidence intervals. The cost estimates were varied by +/- 50%. Some ranges were based on the authors' opinions.

**Estimated benefits used in the economic analysis**

Forty-five perinatal transmissions were avoided per 1,000 births. There was one maternal death per 100,000 deliveries, and 0.02 maternal deaths per 1,000 transmissions avoided. A sensitivity analysis showed that the number of vertical transmissions avoided per 1,000 deliveries varied from 23 to 67. A probabilistic sensitivity analysis showed that the number of maternal death per 1,000 avoided was less than 1 in 65% of cases, and less than 2 in 80% of cases.

Assuming 50% spontaneous HCV clearance in vertically infected infants, the estimated QALE was 42.59 years for the mother and 27.92 years for the infant under current practice. With the RCS, the estimated QALEs were 42.57 (mother) and 28.16 (infant) years, respectively. Assuming 25% spontaneous HCV clearance in vertically infected infants, the estimated QALE was 42.59 years for the mother and 27.53 years for the infant under current practice. With the RCS, the estimated QALEs were 42.57 (mother) and 28.89 (infant) years, respectively.

**Cost results**

Assuming 50% spontaneous HCV clearance in vertically infected infants, the estimated costs were $5,460 with SC and $6,800 with RCS. Assuming 25% spontaneous HCV clearance in vertically infected infants, the estimated costs were $5,510 with SC and $6,840 with RCS.

**Synthesis of costs and benefits**

Incremental cost-utility ratios were calculated to combine the costs and QALYs of the two alternative strategies. The incremental cost per QALY with RCS relative to SC was $6,100 when assuming 50% spontaneous HCV clearance in vertically infected infants, and $3,900 when assuming 25% spontaneous HCV clearance in vertically infected infants.

The sensitivity analyses showed that the results were robust to variations in model parameters such as the maternal QALE and the maternal quality of life decrement associated with C-section. When alternative scenarios were considered, the cost per QALY always remained below the value of $9,100.

**Authors’ conclusions**

Elective Caesarean section (C-section) would result in substantial clinical benefits at an acceptable cost for human immunodeficiency virus (HIV)/hepatitis C virus (HCV)-coinfected pregnant women with suppressed HIV RNA, but detectable HCV RNA, in the USA.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparator was clear. The basic comparator reflected the current pattern of care in the USA. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from published studies. However, it was not stated whether a systematic review of the literature had been undertaken to identify relevant studies. The authors gave details of the design of some primary studies used to provide data. However, specific criteria used to ensure the validity and comparability of the primary sources were not reported. Similarly, the methods used to combine the primary estimates were not described. Some assumptions were also made. The issue of the uncertainty in the model inputs was extensively addressed in the sensitivity analysis.

**Validity of estimate of measure of benefit**
QALYs were used as the summary benefit measure in the economic analysis. This was appropriate as QALYs detect the impact of the interventions on both quality of life and survival. Discounting was performed, as recommended in US guidelines. The source of the utility weights was reported.

Validity of estimate of costs
The authors stated that a societal perspective was adopted, but it appears that only costs relevant to the service provider have been included. Limited information on the unit costs was provided since the costs were presented as macro-categories. The details pertaining to resource use were unclear. The source of the costs was provided. Some cost estimates were varied in the sensitivity analysis. The price year was reported, which aids reflation exercises in other settings.

Other issues
The authors compared their results with those from other studies that had shown the cost-effectiveness of elective C-section among HIV/HCV-coinfected pregnant mothers. The issue of the generalisability of the study results to other settings was not explicitly addressed, although sensitivity analyses were carried out. However, the study focused on US settings. The authors noted some limitations of their study. First, some model inputs were derived from studies performed outside of the USA, which could make the use of such data inappropriate for the US setting. Second, sources that did not make a clear distinction between the results of elective and urgent C-section were used. Finally, antiretroviral therapy was not considered in the model because its impact on the risk of HCV transmission was unclear.

Implications of the study
The study results suggested that elective C-section should be offered to HIV/HCV-coinfected pregnant women with undetectable HIV RNA but detectable HCV RNA. However, the authors stressed that a wide range of factors, in addition to the results of their analysis, should be considered before developing clinical recommendations for HIV/HCV-coinfected pregnant women. The authors noted that future studies should demonstrate an HCV transmission benefit for mothers who had been receiving effective antiretroviral therapy for a long time.

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Other publications of related interest


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