Elective cesarean delivery to prevent perinatal transmission of hepatitis C virus: a cost-effectiveness analysis

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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
Two strategies for the prevention of perinatal transmission of hepatitis C virus (HCV) were examined. One strategy offered an elective Caesarean delivery to HCV-positive women in order to avert perinatal transmission, while the other performed a Caesarean delivery only for obstetric indications.

Type of intervention
Secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of human immunodeficiency virus (HIV)-negative HCV-positive women. HCV positivity was defined as the presence of HCV RNA in maternal blood.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1994 and 2003. The costs and resource use data were obtained from studies published between 1996 and 2002. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies and some assumptions.

Modelling
A decision tree model using a Markov analysis was developed to examine the clinical and economic outcomes of the two approaches under evaluation. The model made several assumptions. First, all HIV-infected neonates who did not spontaneously clear the virus became chronically infected with HCV. Second, all chronically infected neonates had mild hepatitis for a period of 20 years, after which individual could progress to more advanced stages of disease. Finally, disease progression occurred at the same rate as adults infected with HCV. No details were given on the cycle length and time horizon, although it appears that the children's lifetime was considered.

Outcomes assessed in the review
The outcomes estimated from the literature were:
the annual probabilities of disease progression;
the probabilities of elective Caesarean delivery, emergent Caesarean delivery, and vaginal delivery;
the probability of perinatal transmission;
the risk of perinatal HIV infection with elective Caesarean delivery; and
the utility values associated with specific health states.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. No information on the design and characteristics of the primary studies was provided, except for a retrospective study of 441 HCV-infected mothers.

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
Twenty-seven studies provided evidence.

Methods of combining primary studies
A narrative method appears to have been used to combine the primary studies.

Investigation of differences between primary studies
Not stated.

Results of the review
The annual probabilities of disease progression were as follows:

perinatal transmission to spontaneous clearance in first year of life, 10 (range: 0 - 20.0);
mild hepatitis to remission, 0.2 (range: 0.1 - 0.4);
mild hepatitis to moderate hepatitis, 3.0 (range: 2.0 - 4.0);
moderate hepatitis to compensated cirrhosis, 3.0 (range: 2.0 - 4.0);
compensated cirrhosis to decompensated cirrhosis, 3.9 (range: 2.0 - 8.3);
compensated cirrhosis to hepatocellular cancer, 1.5 (range: 0.5 - 2.0);
decompensated cirrhosis to liver transplant, 3.1 (range: 1.0 - 6.2);
decompensated cirrhosis to hepatocellular cancer, 1.5 (range: 1.0 - 2.0);
decompensated cirrhosis to death, 12.9 (range: 6.5 - 19.3);
hepatocellular cancer to death, 42.7 (range: 33.0 - 86.0);
liver transplant to death during the initial year, 21 (range: 6.0 - 42.0);
liver transplant to death during subsequent years, 5.7 (range: 2.4 - 11);
the probability of receiving HCV treatment, 0.7 (range: 0.2 - 1.0); and
the probability of sustained response to treatment, 54 (range: 50 - 58).

With usual care, the probabilities of elective Caesarean delivery, emergent Caesarean delivery and vaginal delivery were
12.3%, 14.5% and 73.2%, respectively. With elective Caesarean delivery, these probabilities were 84.3% (range: 84.3 - 100), 4.3% and 11.4% (range: 0 - 11.4), respectively.

The probability of perinatal transmission was 0% (range: 0 - 7.7) with elective Caesarean delivery and 7.7% (range: 4 - 12) with emergency Caesarean delivery and vaginal delivery. The risk of perinatal HIV infection with elective
Caesarean delivery was 100% (range: 0 - 100).

The utility values were as follows:
remission, 1;
mild hepatitis, 0.98 (range: 0.96 - 0.99);
moderate hepatitis, 0.92 (range: 0.82 - 0.98);
compensated cirrhosis, 0.85 (range: 0.5 - 0.90);
decompensated cirrhosis, 0.6 (range: 0.5 - 0.88);
hepatocellular cancer, 0.25 (range: 0.1 - 0.5);
liver transplant in the initial year, 0.86 (range: 0.6 - 0.9);
liver transplant in subsequent years, 0.95 (range: 0.8 - 0.95); and
treatment, 0.88 (range: 0.82 - 0.91).

Methods used to derive estimates of effectiveness
A panel of experts was convened to assign utility values to each route of delivery.

Estimates of effectiveness and key assumptions
The utility values were as follows:
vaginal delivery, -0.0027 (range: -0.0037 - -0.0017);
elective Caesarean delivery, -0.0035 (range: -0.0045 - -0.0025); and
emergent Caesarean delivery, -0.0046 (range: -0.0056 - -0.0036).
Measure of benefits used in the economic analysis
The summary benefit measure used was the number of quality-adjusted life-years (QALYs). The utility values were obtained from the literature but no details of these sources were given. An annual discount rate of 3% was applied.

Direct costs
Discounting was relevant since the costs were incurred during a long timeframe. An annual discount rate of 3% was used. The costs were presented as macro-categories and a detailed breakdown of the cost items was not reported. The health services included in the economic evaluation were:

delivery costs (elective or emergent Caesarean delivery, vaginal delivery, and infant testing);
management of mild or moderate hepatitis, compensated and decompensated cirrhosis, hepatocellular cancer, remission and liver transplant; and

treatment (48-week course of 800 mg ribavirin in addition to weekly pegylated interferon at 1.5 microg/kg).

The perspective of the health care system was adopted. The costs and resource use were estimated on the basis of published studies and some authors' assumptions. All the costs were inflated to 2001 values using the medical care component of the Consumer Price Index.

Statistical analysis of costs
The costs were treated deterministically.

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

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out on all model inputs to examine the robustness of the cost-utility ratios to variations in the base-case values. Two-way sensitivity analyses were performed on selected parameters. The ranges of values used were presumably derived from the literature.

Estimated benefits used in the economic analysis
Using base-case assumptions, 18 elective Caesarean deliveries would be necessary to avert one case of perinatal HCV transmission.

The estimated QALYs were 29.1821 with elective Caesarean delivery and 29.1487 with usual care (Caesarean delivery performed only for obstetric indications)

Cost results
The estimated costs were $45,814 with elective Caesarean delivery and $4,653 with usual care.

Synthesis of costs and benefits
An incremental cost-utility ratio (i.e. the cost per QALY) was calculated to combine the costs and benefits of elective
Caesarean delivery over usual care. The estimated cost per QALY was $34,812.

The univariate sensitivity analysis showed that the base-case results were sensitive to three model inputs. More specifically, the perinatal HCV transmission rate, the risk reduction attributable to elective Caesarean delivery, and the discount rate. In particular, elective Caesarean delivery was not a cost-effective intervention at relatively low rates of perinatal transmission with emergent Caesarean and vaginal delivery (6.0% or less), or unless elective Caesarean delivery were to reduce perinatal transmission from 7.7% to 1.7% or less (a 77% reduction). It was also not cost-effective if a 5% discount rate was applied (with no discounting, elective Caesarean delivery was dominant).

The two-way sensitivity analysis showed that if perinatal HCV transmission rates were high with emergent Caesarean and vaginal delivery (12%), elective Caesarean delivery needed to reduce transmission rates by only 50% to be a cost-effective intervention. However, if the risk of perinatal HCV transmission was relatively low (6.6% or less) with emergent Caesarean and vaginal delivery, offering elective Caesarean delivery would only be cost-effective if it prevented, at minimum, 90% of HCV perinatal transmission.

**Authors’ conclusions**
Elective Caesarean delivery was a cost-effective strategy for the prevention of perinatal hepatitis C virus (HCV) only if perinatal transmission rates were high, or if it substantially reduced the risk of perinatal HCV transmission.

**CRD COMMENTARY - Selection of comparators**
The selection of the comparators was appropriate since usual care was compared with an alternative approach. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis was based on data obtained from published studies. It would appear that primary studies were identified selectively since details on a review of the literature were not reported. With the exception of one retrospective study, no information on the design and characteristics of the studies was provided. The methods used to examine the comparability of the studies and then combine the primary estimates were not described. Thus, it was difficult to assess the validity of the inputs used. Some assumptions, based on a panel of experts, were also made. However, the approach used to reach consensus was not described. All clinical inputs were varied in the sensitivity analysis, which highlighted the importance of some parameters.

**Validity of estimate of measure of benefit**
The summary benefit measure was appropriate as it captured the impact of the interventions on quality of life and survival. There were no details on the source of the majority of the quality weights, although some data were based on experts’ opinions. The use of QALYs ensures the comparability with the benefits of other health care interventions. Discounting was carried out, as US guidelines recommend.

**Validity of estimate of costs**
The perspective adopted in the study was explicitly stated. As such, it appears that all the relevant categories of costs have been included in the analysis. Since most of the costs were derived from published studies and were presented as macro-categories, a detailed breakdown of the items was not given. This reduces in part the possibility of replicating the analysis. The costs were treated deterministically but the estimates were varied in the sensitivity analysis. The price year was reported, which aids reflation exercises in other settings.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. However, extensive sensitivity analyses, which highlighted the key model inputs, were performed. These increased the external validity of the analysis. The study referred to HCV-positive...
women and this was reflected in the authors' conclusions. The authors noted some limitations of their analysis. First, the model did not include HIV co-infected women. Second, the potential impact of breast-feeding was not considered. Finally, the authors highlighted that the natural history of HCV infection in the paediatric population was not well described in the literature.

**Implications of the study**
The study results suggested that before recommending elective Caesarean delivery, the rates of perinatal transmission stratified by route of delivery need to be further clarified.

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**Other publications of related interest**


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