Routine hepatitis C virus screening in pregnancy: a cost-effectiveness analysis
Plunkett B A, Grobman W A

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
Three strategies for the management of hepatitis C virus (HCV) infection in pregnant women were examined. The strategies were:

- no screening;
- routine HCV screening in pregnancy and subsequent treatment (48-week course of weekly pegylated interferon alfa-2b plus ribavirin) for progressive disease; and
- HCV screening in pregnancy, with subsequent treatment for progressive disease and elective Caesarean delivery to avert perinatal transmission.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of asymptomatic HIV-negative pregnant women without risk factors for HCV infection who received routine prenatal care.

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

Dates to which data relate
The effectiveness evidence was derived from studies published between 1991 and 2003. Some resource use data and costs were derived from studies published between 1992 and 2002. The price year was 2003.

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

Modelling
A decision tree, based on a Markov chain, was constructed to model the natural history of HCV and to examine the impact of the three strategies in a hypothetical 30-year-old pregnant woman. The time horizon of the model was the lifetime of the mother and her child. The cycle length was one year. All women entered the model in the initial health state of mild hepatitis, which was defined as a clinically asymptomatic and histologically mild disease. From this stage, women could enter remission or progress to histologically moderate hepatitis and into more advanced disease states.
(compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, or liver transplant). Women could die due to HCV infection or for non-HCV-related causes. Women who accepted testing were screened initially with a third-generation enzyme immunoassay test that was followed by a confirmatory HCV RNA polymerase chain reaction (PCR). In the arm of the model that evaluated the impact of elective Caesarean delivery, this intervention was offered to all women with positive HCV PCR (although not all women ultimately undergo this intervention, owing to the unpredictability of the onset of labour or rupture of membranes). Medical treatment for HCV infection occurred only after individuals reached the moderate hepatitis health state.

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

the probabilities of receiving HCV treatment in a screened or unscreened population;

the rate of sustained response to treatment;

the acceptance rate of HCV screening;

the prevalence of disease;

the sensitivity and specificity of the tests;

the probabilities of delivery in women with unknown HCV status or in women who screened positive; and

the probability of perinatal transmission by route of delivery.

Transition probabilities and utility values associated with specific health states were also reported.

Study designs and other criteria for inclusion in the review
The authors stated that the clinical inputs were derived from published literature. However, it was not stated whether a systematic review of the literature was undertaken to identify the primary studies. Further, no information on the design of the primary studies was reported.

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
Thirty-eight primary 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
Results of the review
The probability of receiving HCV treatment was 0.2% in the unscreened population and 0.7% (range: 0.2 - 1.0) in the screened population.

The probability of sustained response to treatment was 0.54% (range: 0.50 - 0.58).

The probability of accepting the HCV screening test was 85% (range: 85.0 - 100).

The prevalence of HCV infection was 1% (range: 1.0 - 10.0).

The prevalence of chronic HCV disease was 74% (range: 74 - 85).

The sensitivity of the 3rd-generation enzyme immunoassay was 98.6% (range: 97.0 - 99.9) and the specificity was 99.3% (range: 99.0 - 99.9).

The sensitivity of PCR was 100% and the specificity was 98% (range: 97.0 - 99.0).

In cases of unknown or negative HCV status, the probability of elective Caesarean delivery was 12.3%, the probability of emergent Caesarean delivery was 14.5%, and the probability of vaginal delivery was 73.2%.

In cases of women who screened positive for HCV, the probability of elective Caesarean delivery was 84.3% (range: 84.3 - 100), the probability of emergent Caesarean delivery was 4.3%, and the probability of vaginal delivery was 11.4% (range: 0 - 11.4).

The probability of perinatal transmission by route of delivery was 0 (range: 0 - 7.7) for elective Caesarean delivery, 7.7% (range: 5.9 - 12) for emergent Caesarean delivery, and 7.7% (range: 5.9 - 12) for vaginal delivery.

The following utility values were estimated:

remission, 1;
mild hepatitis (known disease), 0.96 (range: 0.96 - 1.0);
mild hepatitis (not diagnosed), 1;
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 transplantation (initial year), 0.86 (range: 0.6 - 0.9);
liver transplantation (subsequent years), 0.95 (range: 0.8 - 0.95);
treatment, 0.88 (range: 0.82 - 0.91).

Transition probabilities are not reported here.

It was estimated that:

infected neonates remained in the mild hepatitis health state for a latency period of 20 years;
70% of screened women and their children receive treatment upon entering into the moderate hepatitis health state;
for non-screened individuals, only a proportion of the cohort would be diagnosed and treated in a timely fashion;
20% of unscreened patients would receive treatment after reaching the moderate hepatitis health state;
all individuals who had a sustained response entered into a long-term state of remission and did not relapse over the
course of their lifetime;
all women in the screening arm received pre-test counselling; and
only a portion of the women will accept the test.

Methods used to derive estimates of effectiveness
A group of five experts was contacted to determine utility values associated with route of delivery using the time trade-off technique. These values were averaged and assigned as tolls for a 6-week duration (corresponding to the post-partum period).

Estimates of effectiveness and key assumptions
The utility values (tolls for a 6-week duration) were:

-0.0027 (range: -0.0037 - -0.0017) for vaginal delivery,
-0.0035 (range: -0.0045 - -0.0025) for elective Caesarean delivery, and
-0.0046 (range: -0.0056 - -0.0036) for emergent Caesarean delivery.

Measure of benefits used in the economic analysis
The summary benefit measure was the quality-adjusted life years (QALYs). These were calculated by combining survival data with quality of life estimates. Both series of data were derived from the literature and estimated using the decision model. An annual discount rate of 3% was applied.

Direct costs
The costs were discounted at an annual rate of 3% since the lifetime costs were estimated. The unit costs were presented separately from the quantities of resources used only for some items. The health services included in the economic evaluation were pre- and post-test counselling (distinguishing between positive and negative results), screening tests, delivery procedures, and annual costs associated with the management of patients in the different health states. The cost/resource boundary of the study was that of the health care system. The resource use data were derived from authors' assumptions and published evidence. All the costs came from published studies. The costs were inflated to 2003 values using the medical care component of the Consumer Price Index.

Statistical analysis of costs
No statistical analyses of the costs were carried out.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).
Sensitivity analysis
Univariate and multivariate sensitivity analyses were carried out on clinical and economic inputs. These examined the cost-effectiveness of the base-case results (cost per QALY) to variations in baseline values. The ranges of values used were generally derived from published sources. Further, 10,000 simulation trials were run and the results were compared with longitudinal data on HCV infection from five prospective cohort studies and other published models.

Estimated benefits used in the economic analysis
The estimated QALYs (mother and child) were 54.48958 with no screening, 54.48947 with screening with treatment, and 54.48968 with screening with treatment and Caesarean delivery.

Cost results
Per patient costs were $4,552 with no screening, $4,660 with screening with treatment, and $4,669 with screening with treatment and Caesarean delivery.

Synthesis of costs and benefits
An incremental cost-utility ratio was calculated to combine the costs and benefits of the alternative screening strategies. The incremental analysis revealed that screening with treatment was dominated by no screening, which was both more effective and less costly. The incremental cost per QALY gained with screening with treatment and Caesarean delivery over no screening was $1,170,000. In particular, when the analysis was performed separately for the mother and the child, the strategy of screening with treatment was dominated by no screening from both perspectives. The addition of Caesarean delivery only adds to the maternal costs and decreases utility because of the disutility of Caesarean delivery itself. However, for the child, the prevention of HCV transmission by Caesarean delivery adds only $0.54 and improves total effectiveness by 0.00018 QALY, for a cost-effectiveness ratio of $3,019 per QALY relative to the current strategy of no screening.

The sensitivity analyses (both one- and two-way) showed that the current standard of care (i.e. no screening) remained the most cost-effective strategy in all scenarios considered in the analysis. None of the other screening strategies were cost-effective (given a threshold of $50,000 per QALY) even when favourable assumptions were made.

Authors' conclusions
When conventional threshold for health care interventions were used, screening pregnant women for hepatitis C virus (HCV) and subsequent treatment for progressive disease were not cost-effective and were dominated by the current practice of no screening.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparators was clear since usual care (i.e. no screening) was compared with two screening strategies. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from the literature. Details on the methods and conduct of the review were not reported. It was not explicitly stated whether the review of the literature was systematic. Further, information on the design of the primary studies was reported only for some inputs. Differences between the primary studies were not investigated and the validity of the primary sources was not addressed. The approach used to combine the primary estimates was not described. Some utility values were derived from experts' opinions. Owing to the uncertainty around some estimates, an extensive sensitivity analysis was performed on all model inputs.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate as they incorporate the two most relevant dimensions of health (quality of life and survival). The utility values were derived from the literature as well as experts’ opinions. Discounting was performed, as recommended in US guidelines. QALYs are comparable with the benefits of other health care interventions.

Validity of estimate of costs
The categories of costs included in the analysis were consistent with the perspective adopted in the study. The authors stated that the inclusion of the indirect costs would have been interesting, although such costs are likely to represent only a small proportion of the total lifetime costs for a minority of the population. The unit costs were not presented separately from the quantities of resources use for all items, as some costs were given as macro-categories. This limits the possibility of replicating the results of the analysis in other settings. The source of the data was reported. The costs were treated deterministically, but the economic estimates were varied in the sensitivity analysis. The price year was reported, which aids reflation exercises.

Other issues
The authors did not compare their findings with those from published studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. Extensive sensitivity analyses were carried out, but the results were presented selectively. The study referred to the general population of pregnant women and this was reflected in the authors’ conclusions. The authors noted some limitations of their analysis. For example, the lack of published evidence on some utility values and the use of limited evidence on the natural history of HCV infection in a paediatric population. Some strengths of the analysis were also noted. For example, the robustness of the conclusions, the appropriate time horizon of the model, and the validation of the Markov model.

Implications of the study
The study results supported the current no screening strategy for HCV detection in asymptomatic pregnant women. The authors stated that, in the future, new treatments might offer the possibility that screening would become a cost-effective intervention.

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