Cost-effectiveness of induction after preterm premature rupture of the membranes
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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
A protocol for the management of induction after preterm premature rupture of the membranes (PPROM) between 32 and 36 weeks' gestation was examined. The protocol was immediate delivery or prolonged gestation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with PPROM between 32 and 36 weeks' gestation.

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

Dates to which data relate
Effectiveness evidence came from studies published from 1988 to 1996 and from 1992 to 1997. The resource use data were estimated in 1996. The price year was 1996.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies, a database and one key assumption.

Modelling
A decision model, based on a decision tree, was constructed to assess the clinical and economic outcomes associated with the strategies under evaluation. Five separate models were considered, one for each gestational age from 32 to 36 weeks. No patients were allowed to stay pregnant after 36 weeks' gestation. After a decision to deliver at a given time was made, the model considered the probabilities of delivering in the previous weeks. The model considered only neonatal outcomes on the effectiveness side, while both maternal and neonatal outcomes were considered in the cost analysis. For each planned latency, there were four possible neonatal outcomes. More specifically, no morbidity, infectious morbidity resulting from latency, and major and minor morbidity resulting from gestational age. The structure of the tree for the model at 34 weeks' gestation was reported in the paper.

Outcomes assessed in the review
The outcomes estimated from the published studies were:
the probability of delivery after rupture of the membranes at between 28 and 36 weeks' gestation, depending on the latency period for women who received antibiotics; and

the probability of neonatal mortality and morbidity.

**Study designs and other criteria for inclusion in the review**
A review of the literature does not appear to have been conducted. The evidence for the probability of delivery was derived from a randomised trial, the results of which were compared with those from three other clinical trials. The probability of neonatal mortality and morbidity was obtained from a sample of 121 maternal-neonatal pairs, as identified from the birth log database at the author's institution (the Beth Israel Deaconess Medical Center).

**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**
Five primary sources provided the evidence.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The probability of delivery after rupture of the membranes between 28 and 36 weeks' gestation for women who received antibiotics was:

- 12.5% for less than 1 week of latency,
- 50% for 1 week of latency,
- 8.3% for 2 weeks' latency, and
- 4.2 for 3 or 4 weeks' latency.

The neonatal mortality rate was 0%.

Latency morbidity was not reported.

**Methods used to derive estimates of effectiveness**
The author made a key assumption about latency morbidity.
Estimates of effectiveness and key assumptions
It was assumed that latency morbidity was only due to infectious morbidity and was independent of gestational age.

Measure of benefits used in the economic analysis
The summary benefit measure was the rate of neonatal morbidity averted. This was derived from the decision model.

Direct costs
Discounting was not relevant since the costs were incurred during a short time. The unit costs and the quantities of resources used were not presented separately. The economic evaluation comprised maternal and neonatal costs, including all hospital services delivered at the Beth Israel Deaconess Medical Center. The Beth Israel Deaconess Medical Center provided both the costs and resource use data. A sample of 55 maternal-neonatal pairs was used. The neonatal costs were based on gestational age at delivery and were divided according to major, minor, or no morbidity. The cost/resource boundary of the hospital was adopted. The costs were expressed in 1996 values.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
With PPROM at 32 weeks' gestation, the morbidity averted was 0.6667 with deliver now, 0.7708 with deliver in 1 week, 0.5898 with deliver in 2 weeks, 0.6959 with deliver in 3 weeks, and 0.7792 with deliver in 4 weeks.

With PPROM at 33 weeks' gestation, the morbidity averted was 0.7857 with deliver now, 0.8937 with deliver in 1 week, 0.6778 with deliver in 2 weeks, and 0.7750 with deliver in 3 weeks.

With PPROM at 34 weeks' gestation, the morbidity averted was 0.9091 with deliver now, 0.9886 with deliver in 1 week, and 0.7386 with deliver in 2 weeks.

At 35 and 36 weeks' gestation, no major morbidity occurred and there was no benefit in delaying delivery. Thus, the most beneficial strategy at 35 and 36 weeks' gestation was deliver now.

Cost results
With PPROM at 32 weeks' gestation, the estimated costs were $6,580.14 with deliver now, $4,920.73 with deliver in 1 week, $5,161.89 with deliver in 2 weeks, $5,243.67 with deliver in 3 weeks, and $5,409.47 with deliver in 4 weeks.

With PPROM at 33 weeks' gestation, the estimated costs were $3,495.96 with deliver now, $3,509.87 with deliver in 1 week, $3,911.52 with deliver in 2 weeks, and $4,069.95 with deliver in 3 weeks.
With PPROM at 34 weeks' gestation, the estimated costs were $2,325.79 with deliver now, $2,885.03 with deliver in 1 week, and $3,270.21 with deliver in 2 weeks.

The costs estimated at 35 and 36 weeks' gestation were not reported.

**Synthesis of costs and benefits**

The average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative strategies.

With PPROM at 32 weeks' gestation, the average cost per averted episode of morbidity was $9,870 with deliver now, $6,384 with deliver in 1 week, $8,752 with deliver in 2 weeks, $7,535 with deliver in 3 weeks, and $6,942 with deliver in 4 weeks.

With PPROM at 33 weeks' gestation, the average cost per averted episode of morbidity was $4,450 with deliver now, $3,927 with deliver in 1 week, $5,771 with deliver in 2 weeks, and $5,252 with deliver in 3 weeks.

With PPROM at 34 weeks' gestation, the average cost per averted episode of morbidity was $2,558 with deliver now, $2,918 with deliver in 1 week, and $4,427 with deliver in 2 weeks.

With respect to the incremental analysis, the author reported the results of the alternatives that were not dominated (less effective and more costly).

With PPROM at 32 weeks' gestation, the incremental cost-effectiveness ratio of deliver in 4 weeks over deliver in 1 week was $58,117.

With PPROM at 33 weeks' gestation, the incremental cost-effectiveness ratio of deliver in 1 week over deliver now was $129.

With PPROM at 34 weeks' gestation, the incremental cost-effectiveness ratio of deliver in 1 week over deliver now was $7,032.

The cost-effectiveness ratios at 35 and 36 weeks' gestation were not reported.

Assuming that there were 1,000 cases of PPROM between 32 and 34 weeks (divided evenly for each gestational age), when using the most cost-effective strategy (deliver in 1 week) the costs were $3,772,000 and there were 115 cases of neonatal major morbidity.

The common practice of inducing labour at or around 34 weeks' gestation led to $106,000 cost-savings. However, it resulted in 87 additional cases of major morbidity.

If all women delivered at 35 weeks' gestation, the extra costs would be $242,000 and there would be 97 additional cases of major morbidity.

If all women delivered at 36 weeks' gestation, the extra costs would be $478,000 and there would be 120 additional cases of major morbidity.

However, if all patients delivered immediately after ruptured membranes, the extra costs would be $362,000 and there would be 98 additional cases of major morbidity.

**Authors' conclusions**

The most cost-effective strategy was to deliver in 1 week between 32 and 34 weeks' gestation and to deliver immediately after 35 weeks' gestation. The implementation of such a strategy led to an extra cost of $106,000, but resulted in 87 fewer cases of major neonatal morbidity.
CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The range of strategies covered almost all possible options for the management of PPROM. One of the strategies reflected current practice at the author's institution. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came mainly from completed studies. However, a systematic review of the literature does not appear to have been conducted. The design of the primary sources was reported. The methods used to extract and combine the primary estimates were not given. A key assumption was also made. The issue of uncertainty around the effectiveness estimates was not investigated in the sensitivity analysis. This reduced the validity of the study.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the intervention considered in the study and would be difficult to compare with the benefits of other health care interventions. The use of a more generalisable measure would have been helpful.

Validity of estimate of costs
The author stated the perspective that was adopted in the study and only hospital costs were included in the analysis. However, a detailed breakdown of the cost items was not reported and information on the unit costs and quantities of resources used was not provided. This reduces the possibility of replicating the study in other settings. The costs were derived from a single institution and were specific to the study setting. No sensitivity analyses were conducted to deal with the issue of variability in the data. The costs were treated deterministically. The price year was reported, thus facilitating reflation exercises in other settings. The cost analysis did not consider multiple morbidity episodes since only the most severe were included in the analysis. This could, therefore, have underestimated the real costs of the service.

Other issues
The author reported the results of other published studies that assessed the clinical and economic outcomes associated with premature labour. In terms of the generalisability of the study results to other settings, the author noted that most of the clinical evidence and economic data came from a large tertiary care centre, thus the results should be applicable to similar centres. Sensitivity analysis was not conducted, and this will have affected the external validity of the analysis. The author noted some limitations to the validity of the analysis. First, the use of a relatively small database that referred only to a timeframe of 2 years. Second, maternal outcomes were not included in the analysis. Finally, 1-week intervals were considered in the model but a shorter interval, such as 48 hours, could have been relevant.

Implications of the study
The author suggested that hospitals and insurance systems should consider implementing protocols for the management of women with PPROM to reduce major neonatal morbidity, despite the higher costs.

Source of funding
None stated.

Bibliographic details

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Other publications of related interest

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